

# The Pseudo-ulcer



## Ulcer-like symptoms: no G.I. pathology

The patient is convinced it's an ulcer. However, symptoms are not quite typical, and x-ray findings are negative. These findings and the results of additional diagnostic procedures exclude an organic basis for the patient's complaints. A diagnosis of "upper functional gastrointestinal disorder" is made, which is supported by the fact that episodes of painful symptoms coincide with episodes of excessive anxiety, as indicated by the history.

It may be useful to explain to the patient the mechanism by which emotions upset normal G.I. functioning, resulting in hypersecretion and hypermotility and thus causing such symptoms as nausea and epigastric pain. In upper functional gastrointestinal disorders, counseling by the primary physician can often help the patient to understand how excessive anxiety may cause flare-ups of G.I. symptoms.

A disproportionate number of patients seen by the general practitioner suffer from functional disorders, as do more than half of those seen by the gastroenterologist.\* Where milder cases may respond to counsel-

ing alone, if symptoms are severe and disabling to any degree, a suitable regimen may include medication to reduce the symptoms and the excessive anxiety that often provokes these distressing symptoms.

In these cases, Librax as an adjunct can greatly contribute to the course of therapy. Its dual action can offer relief of both painful symptoms and excessive anxiety, because each capsule contains 5 mg chloridazepoxide HCl and 2.5 mg clidinium Br. The antianxiety action of Librax (chloridazepoxide HCl) makes Librax exceptional among drugs for certain gastrointestinal disorders associated with excessive anxiety; the clidinium bromide (Quarvan®) component furnishes dependable antisercretory-antispasmodic action. Dosage is flexible; it may be adjusted according to your patient's requirements within the range of 1 or 2 capsules three or four times daily, up to 8 capsules daily in divided doses.

\*Rome HP, Brannick TL. Orientation and mechanism of functional disorders: clinical-physiological correlation, chap. 133, in *Gastroenterology*, edited by Bodum HJ. Philadelphia, WB Saunders Company, 1965, p. 1115

An adjunct in anxiety-related upper functional G.I. disorders

### Librax®

Each capsule contains 5 mg chloridazepoxide HCl and 2.5 mg clidinium Br.

Before prescribing, please consult complete product information, a summary of which follows

**Indications:** Symptomatic relief of hypersecretion, hypermotility and anxiety and tension states associated with organic or functional gastrointestinal disorders; and as adjunctive therapy in the management of peptic ulcer, gastritis, duodenitis, irritable bowel syndrome, spastic colitis, and mild ulcerative colitis.

**Contraindications:** Patients with glaucoma, prostatic hypertrophy and benign bladder neck obstruction; known hypersensitivity to chloridazepoxide hydrochloride and/or clidinium bromide.

**Warnings:** Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence has rarely been reported on recommended doses, use caution in addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in

pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards. As with all anticholinergic drugs, an inhibiting effect on lactation may occur. Precautions in elderly and debilitated, limit dosage to smallest effective amount to preclude development of ataxia, overexcitation or confusion (but more than two capsules per day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potent adverse usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, agitation, patients). Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies; and other depressive reactions. Adverse effects have been reported in patients receiving the drug and oral anticholinergic agents. Adverse reactions have not been established clinically.

Adverse reactions: No side effects or manifestations not seen with either compound alone have been reported with Librax. When chloridazepoxide hydrochloride is used alone, drowsi-

ness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances symptoms have been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reductions; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis, leukopenia and hemophilia) have been reported occasionally with chloridazepoxide hydrochloride, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax are typical of anticholinergic agents, i.e., dryness of mouth, blurring of vision, urinary hesitancy and constipation. Constipation has occurred more often when Librax therapy is combined with other antispasmodics and/or low residue diets.



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Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110

making rounds at press time

## Cytomegalovirus Infections At Birth Linked to Low IQs

By FRANCES GOODNIGHT  
Medical Tribune Staff

NEW YORK—Follow-up studies of young children who had at birth excreted cytomegalovirus (CMV) have shown that such congenital infection is associated with lower IQs than the levels found among matched or random controls, and may also be "a significant cause" of profound deafness.

These findings emerged from detailed examinations of 44 children tested 3.5 to seven years after their birth, Dr. James B. Hanshaw, of the University of Rochester School of Medicine and Dentistry, reported here.

The study population included all but nine of the 53 infants discovered to have cord sera positive for CMV-IgM antibody when 8,644 consecutive sera specimens were tested at a Rochester hospital between 1967 and 1970. One positive infant had lived only a short time, another was stillborn, and the remaining seven positives were unavailable for examination.

Most children with congenital CMV infection are asymptomatic in the newborn period and fewer than 5 per cent exhibit clinical signs that arouse suspicion of CMV infection. Dr. Hanshaw emphasized at a symposium presented by the New York University School of Medicine during the newborn period, according to Dr. James Hanshaw.



A patient with congenital cytomegalovirus infection detected by screening of cord serum for CMV-IgM antibody. The patient is microcephalic, hypotonic, and deaf, and has psychomotor retardation. No abnormalities were noted during the newborn period, according to Dr. James Hanshaw.

## Complications No Matter

### CPK Isoenzyme Sensitive Index Of Infarct's Size

Medical Tribune Report

HOUSTON—The size of a myocardial infarct can be evaluated accurately even in patients with complicated infarction by analyzing serum values of one isoenzyme of creatine phosphokinase (CPK), the American College of Cardiology was told here.

Investigators at Washington University School of Medicine said that this "MB" isoenzyme is found primarily in myocardium and thus provides a "sensitive and more specific index of myocardial damage than total CPK," which reflects release of enzyme from non-cardiac sources.

They noted that noncardiac CPK may influence serum activity after intramuscular injection, hypotension, or shock.

In a separate report, members of the research group also presented evidence that assays of the MB isoenzyme in serum samples from patients undergoing cardiac catheterization can distinguish the CPK elevations accompanying these procedures from CPK elevations associated with myocardial infarction.

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## MD Resistance to PSROs Dying—Simmons

By EDWARD GROSSMAN  
Medical Tribune Staff

NEW YORK—If the network of Professional Standards Review Organizations, plans for which must be submitted in 203 districts nationwide by Jan. 1, 1976 runs into trouble, it won't be because of resistance or non-cooperation on the part of physicians, according to Dr. Henry E. Simmons, Deputy Assistant Secretary of Health.



DR. SIMMONS

It will be on account of budgetary cuts piling many government projects. Despite the cuts, the Office of Professional Standards Review of H.E.W. will soon announce a new funding cycle that will expand the program and allow 50 to 60 new districts to join the more than 90 in which compliance plans submitted by physicians have been approved and awarded contracts, and 13 in which PSRO is actually in operation. This guardedly optimistic forecast

for PSROs was made by Dr. Simmons during an interview with MEDICAL TRIBUNE.

"Resistance is rapidly dying out among physicians, and no wonder," Dr. Simmons said. "By and large they realize that PSRO is their best, and maybe last, chance to have a hand in improv-

ing health care without compromising their professional standing and responsibility."

"The proof of this is that increasing numbers of districts are giving us their plans, and many state medical societies that had previously been opposed have

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## Survey Finds Little Change In Clinician Use of Rauwolfia

By HARRIS PAGE  
Medical Tribune Staff

NEW YORK—Clinicians appear not to have made any substantial changes in their use of rauwolfia derivatives, such as reserpine, in the wake of conflicting studies concerning links between these drugs and cancer, MEDICAL TRIBUNE found in telephone interviews.

These studies have, in the past six months, claimed an association between the use of rauwolfia derivatives and breast cancer, showed no association between the use of rauwolfia and cancer, and left hanging the possibility of a connection between hypertension and cancer.

Dr. Rita Kelly, a medical oncologist at Massachusetts General Hospital, summed up the situation as "muddy." She has not seen any relationship between rauwolfia compounds and cancer in her patients and, she said, "I have not stopped reserpine in women who have had breast cancer and have been on the drug for a long time, and who are under good control with the reserpine, because hypertension is a bad disease, too."

She is inclined to view the retrospective studies in general as "not terribly helpful," she said. "The correlation in

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## Ind. MDs Look to Panel Plan To Relieve Malpractice Bind

By MICHAEL HERRING  
Medical Tribune Staff

INDIANAPOLIS—Indiana physicians, facing the uncertain future of choosing between malpractice insurance premiums of \$18,000 to \$25,000 a year, or none at all, are working with the state legislature to enact measures that will hopefully eliminate unfairness in malpractice litigation.

A bill calling for the formation of pretrial screening panels—special teams of three doctors who will review malpractice suits and present their findings to a court of law—is before the state Senate, according to Dr. Paul F. Miller, co-chairman (with Dr. Bill Cast) of the State Medical Association committee supporting the bill's passage.

### Makeup of Panel

The panels would consist of one doctor chosen by the plaintiff, one by the defendant, and a third by the first two panelists. Dr. Miller told MEDICAL TRIBUNE, in cases of dispute over panelists, the court may appoint all three.

"The panelists are subject to subpoena as witnesses in the jury trial, and their decision is admissible as evidence in court by either party in the suit," he added.

Under the bill, only the first \$100,000 of any award is paid by the physician's insurance, thus setting a cap on insurer losses. Dr. Miller explained. A patient may win up to \$400,000 more, he said, but this portion of any judgment will be paid from a special "catastrophic fund," with money provided by a 10 per cent surcharge on all malpractice insurance policies in the state.

The bill passed by the House originally called for a full-time Patient's Compensation Board—two physicians, two attorneys, and two lay people who would hear and decide all malpractice cases in the state. The members were to be nominated by state bar and medical associations and appointed by the Governor. This bill was to guarantee full payment to the patient of any award up to \$100,000, make attorney fees independent of plaintiff award, set a cap on insurance payments, and prevent subrogation by the patient's health insurer. Expert witnesses were built into this plan and an additional \$100,000 maximum award for catastrophic cases would be paid from a fund maintained by the local medical community. Dr. Miller told MEDICAL TRIBUNE.

### Elimination of Nuisance Cases

"The big value of the panel is the elimination from the courts of nuisance cases," Dr. Miller said. As soon as the panel labels a case "nuisance," the plaintiff's attorney will give it up, knowing this will be introduced as evidence.

"In the past attorneys have submitted cases without merit because they know the insurance companies won't fight them and will settle out of court for some minimal payment. This has driven up insurance rates and slowed down the whole legal process."

"I think very few cases will go to court under the new bill. If a case is meritorious, both attorneys now know

there's a limit to what they can win or lose in court, so I think they'll settle beforehand. Either way, a case may now be decided in two to four months, rather than years," he said.

Dr. Miller, who is Medical Director of St. Vincent's Hospital here, also nullified other features of the bill:

- Liability of two years for adults, and two years after the age of six for children. After this, the doctor is no longer responsible for the patient's well-being.
- No more "ad damnum" or "breach of warranty" suits. The former (loosely translated, "the prayer") is the "half-a-million-dollar suit that hits the headlines and makes the doctor look horrible," Dr. Miller explained. Now the patient may sue only for damages, not a sum of money, and this will not receive much public notice, he said.

A "breach of warranty" suit occurs when a doctor has tried to assure a patient in distress by saying, "Don't worry, we'll take care of you." Then he is sued on the grounds that he guaranteed that the patient's disease could be cured. Dr. Miller said. "Now they can't sue for that unless the doctor puts this in writing and no doctor would dare do that."

While he believes that "there's no opposition to the bill at this point," and expects it to become law this week, Dr. Miller concluded, "It's not law yet—and there's many a slip between the cup and the lip."

### Egberg Applauds Effort

Dr. Roger O. Egberg, Special Assistant to H.E.W. Secretary for health policy and assigned to the national problem of physician insurance, attended hearings for the Indiana bill. "I was amazed at how far they've gotten in Indiana," he told MEDICAL TRIBUNE. "Their interest and sense of responsibility in taking hold of the issue on a local level is the key to the overall problem. It should be handled by individual states, unless there is a breakdown in getting insurance. Then

## Coronary Prevention Project Visits Congress



Dr. John LaRosa, left, director of Coronary Prevention Project at George Washington University Medical Center, takes blood pressure of Rep. Les J. Ryan during coronary risk factor testing of House and Senate members, sponsored by Rep. Walter E. Fauntroy and Senator Charles M. McNair.

the federal government will have to step in."

In summing up the causes of so many recent suits against physicians, Dr. Egberg listed the following points:

- Advocates la Medicine. Announcements of these created "an unduly hopeful image of what doctors can do. Some think doctors can interfere with the laws of nature, ironically, the more advanced the specialty, the greater the danger that a patient will be disappointed."

● Specialization. Specialists may see a patient only a few times in an atmosphere not necessarily conducive to good rapport and understanding. "The specialist is the expert, but many have forgotten they are dealing with a person."

● Change in public attitude. Partly from advances in medicine, partly from news of other malpractice suits, "many people have developed the attitude: 'Maybe I'm missing something.'"

● Physician shortage. "The physician's average income in 1943 was \$3,000. Today people see doctors as pretty damn well off, which they are. This has created a lack of sympathy for them as a group. They are also a powerful group."

● Insurance. "Patients know doctors are insured into the millions."

● Legality. "Long-tail liability, abuse of res ipsa loquitur, changes in legal trends generally, have increased insurance premiums and raised the cost of health care."

● Attorney fees. The number of suits, as well as the average judgment, is going up 10 per cent a year. "Public expectation is constantly excited."

● Image of perfection. "Many doctors won't admit they made a little mistake or had an accident, especially in hospital settings. In addition, the more sophisticated the techniques, the more opportunity for a slip-up that may turn into a catastrophe."

Dr. Egberg described federal plans to look more closely at the five or six million unexpected incidents that occur annually in hospitals. "The insurance reports don't tell us enough," he said. "We want to find out more about what actually caused these little accidents, what was to blame, and what was done about it."

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## Pediatrician-Internist Team Plan Founders

Medical Tribune Report

STANFORD, CALIF.—"A tremendous number of unforeseen problems" will force the termination next July—at least in its present form—of an unusual primary care residency program at the Stanford University School of Medicine.

These problems, explained Dr. Court Gibson, who is chairman of the Department of Family, Community, and Preventive Medicine, have sent him back to the drawing board to design an alternative program for the one which, as presently set up, brings together residents in pediatrics and internal medicine to work in pairs to provide primary health care for a panel of families over a three-year period.

### 4 Residents in Program

Four residents have been involved in the program, which began last July and is centered in a nearby community health center, rather than the hospital's outpatient departments.

Dr. Gibson sees the problems, frustrating though they have been, as "challenges which require response and solution."

He identified and described some of the major problems which have led to termination of the present program:

Although the heads of the departments of pediatrics and internal medicine supported the collaborative project, no model for the kind of "diadic relationship" proposed existed among faculty members. It proved difficult to develop a working relationship among the residents which did not already exist among faculty members to some degree.

Primary care residents were also part of regular residency programs and "were pulled and tugged away from primary care commitments."

### Problems at Health Center

Vacation schedules, for instance, were woven in with the schedules of other internal medicine and pediatrics residents so that one or another of the primary care residents was on vacation for four of the program's first six months.

Also, the chiefs of in-patient services through which the residents rotated have been reluctant to release the primary care residents for a half day to allow them to follow their panel of families, since "the resident on a sophisticated medical ward has become a crucial part of the functioning of the ward."

And some of the rotations were up to 25 miles away from Stanford, creating additional time problems for the primary care residents with their extra commitment.

The community health center where the primary care training is based has had a number of organizational and governing problems, "which might be challenging and stimulating during a six to eight week rotation but don't provide the stable base needed for the training environment of a resident over a three-year period."

The members of the community served by the center were not accustomed to the family-centered approach to primary health care. Family members saw no need to come when they

were not sick and were reluctant or found it difficult to bring in an entire family, sick or well.

Also, the most convenient time for an entire family to come was after 5 p.m. when the regular staff of the center was gone and no assistance was available from technicians, social workers, dentists, and others.

A resolution of these problems will produce a new approach to primary care training, Dr. Gibson predicted. He plans to recommend the development of a family practice program, based in a community institution so that the program can be "person, family, and community centered."

The present primary care residency brought together two of the elements Dr. Gibson believes are concerned with primary care, as a pediatrics resident worked with an internal medicine resident in a community health center.

But while the program involved the traditional medical school departments and the community medicine/consumer movement, it did not involve the family practice movement, the third of the separate and distinct, but interacting, groups involved in primary care, he said.

### 'Paculiarities' in Training

Although many internists and pediatricians consider themselves primary care specialists, Dr. Gibson maintained that some "peculiarities" in their training make them ill-equipped to provide primary care. He defined primary care as a continuous, broad relationship between patient and physician, not confined to a particular disease but encompassing such elements as early diagnosis, disease prevention, the primacy of health, assistance in convenience and provision of comfort to the dying.

The teaching hospital, which was the incubator for its modern science of medicine, has produced a group of highly educated, hospital-oriented professionals whose specific focus on the lesion has given rise to more and more subspecialties and has produced a

steady drop in the number of professionals interested in primary care," he said.

The training of internists, for instance, is hospital-based and focused on the diseases, not the person, he explained. And, although half of the problems encountered in primary care are emotional, internists have little training in dealing with emotional problems, and they have none in the growth and development of children and adolescents, he said.

Pediatricians do have some training in dealing with emotional problems but they don't deal with these in a family setting for they give little attention to the father and none to the elderly, Dr. Gibson continued.

Since antibiotics and immunization have changed the type of care provided by pediatricians, "the monotonous aspects of office practice and low financial rewards are making pediatricians an abandoned specialty," he added.

### Wearable Tonometer



A plastic ring containing a small pressure transducer that can be worn under the eyelid to monitor eyeball pressure has been developed at the University of Utah. The new system was developed to aid in the research and treatment of glaucoma.

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CLINICAL NEWS NOTE: "Eventually, I expect there will be a uniform system of reviewing all hospital patients, whether their bills are being picked up by the government or third party private insurers, and irrespective of when or whether we get national health insurance. I don't rule out the possibility that one day outpatients will be covered, too." (Dr. Henry E. Simmons, see page 15.)

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## Hospital Computer Converted From a 'Redundant Secretary'

By RALPH COSHAM  
Special Tribune Correspondent

TUCSON, Ariz.—Physicians and computer scientists at the San Diego VA Hospital have devised a system that has turned their computer from a "redundant secretary" into a useful tool that has helped improve patient care in the hospital's surgical intensive care unit.

Dr. A. G. Greenburg of the Department of Surgery, University of California, San Diego, said the new system was designed after an evaluation study showed the computer was underutilized "primarily because it was not useful."

"The output of the original monitoring system was ignored by the nurses because they distrusted the data or had to work too hard to obtain that which

they already knew, and rejected by the physicians because it represented information they did not need," he said.

Dr. Greenburg said the new system was designed to provide instruction and advice for all personnel, on all aspects of patient care, while attempting to maximize use of the computer.

"We have developed or implemented programs that are both instructive and advisory. Our objective has been to provide easily obtainable, explicit information about specific problems."

With the new system, given a physiologic subsystem and a particular variable, personnel can find out:

- whether or not the variable is deviant;
- obtain a list of probable causes for the deviation;

- obtain an explanation of the pathophysiology of particular deviants as well as instruction on how to identify a most probable cause; and
- how to correct specific deviants.

The new system resulted in an immediate and sustained increase in computer utilization, Dr. Greenburg said.

"As a result, we have a better educated staff who communicate more effectively, deal with more sophisticated information, and make better decisions with resultant improved patient care."

Dr. Greenburg's co-workers in the development of the computer system were a computer scientist, D. K. McClure; an information systems analyst, R. Fink; J. A. Stubbs, R.N.; and Dr. G. W. Peskin.

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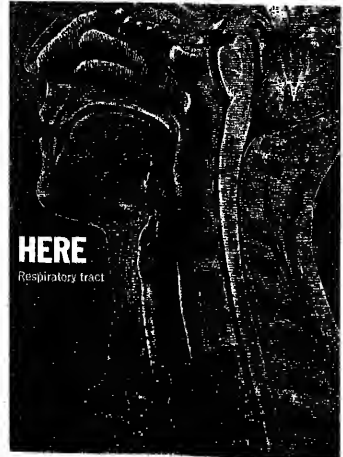


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## EDITORIAL CAPSULES

Brief summaries of editorials or comments in current medical and scientific journals.

### Provide and Conquer

... our clouded and crazed crystal ball has come up with a prediction of a future move by H.E.W. (as the generic drug thing becomes an established way of life).

"Aux laboratoire, mes amis!"

"With hardly a change in script, the agency can mount the attack. What is the first cry that greets us each day?"

Health care costs are outrageously high and climbing. Clearly something must be done and the doing can best be accomplished in relation to the case with which a given area of cost can be identified. To the bureaucratic mind, laboratory service should be a natural. Here is a significant segment of medical care cost for which a monetary figure can be derived from hospital bills, insurance reports, published fee schedules, and the guesses, educated and otherwise, that go into the development of such figures. This can be brought to the public attention with appropriate implications that there must be something awfully about anything that costs that much.

"A standard feature of the bureaucratic approach, gleefully picked up by the Sunday supplement, is the exposure of the unconscionably excessive or inappropriate use of the thing it wishes to control. Someone will 'expose' the fact that many laboratory procedures enjoy the sanctity of being called 'routine,' which often means, in fact, that its value is dubious but which will be interpreted as meaning that no distinct benefit to a particular patient can be demonstrated and it was therefore unnecessary.

"...the laboratory service...is, to the patient, a relatively detached and impersonal activity as compared with his intimate relationship with the physician. We admit to the conviction that it is only the force of this relationship which has spared the clinician from a more complete invasion of his office than already exists. So far, the public has, perhaps unconsciously, resisted this invasion because the physician's private office or the hospital bed—has been the point of personal contact with the physician, the focus of the private and personal character of the process, the place where he is an individual rather than a unit of contribution.

"In short, the method is relatively simple. Establish control over those services that are peripheral or those with a distinctive social appeal. Don't work directly on old Doc Yak because the public still has kindly feelings for him, but pick off his ancillary services one at a time by agency resolution—a tidier and more effective approach in the long run than legislative confrontation. But the physician has—or should have—the uneasy feeling that when enough of his satellites have been brought under federal control so, to all intents and purposes, will he be. (Editorial Comment, David E. Gray, M.D., J. Kans. M.S., 76:42, Feb., 1975)

## IN CONSULTATION

### What is new and important in food allergy?



#### The Consultant

Dr. CLAUDE A. FRAZIER, M.D., F.A.C.A.

Author of *Coping with Food Allergy*, published by Quadrangle Books, New York Times Publishing Co., New York; and *Immunology*, published by Medical Examination Publishing Co.

I HAVE BECOME intrigued recently by two phases of allergy that are receiving much attention these days—the possibility that allergy to food is far more prevalent than hitherto imagined, and the role of emotional stress in allergy diseases. In a way, the two now and then touch upon the same plane since allergy

to food can produce symptoms so diffuse and so nebulous as to be easily dismissed as being neurotic in origin. And the emotional stress of a patient so summarily dismissed who *knows* he does not feel well, who *knows* that something is wrong, can be imagined. Not only this, but allergy to food can cause some strange central nervous system symptoms such as confusion, irritability, depression, extreme fatigue, poor coordination and the like; all of which may create a bit of skepticism in the attending physician.

It is very important for the physician to know the botanical relationship of foods (cashew nuts, pistachio nuts and mangoes are all in one family) and also where a person may come in contact with a food (peanut oil is sometimes used in cooking doughnuts) and give this knowledge to his patients.

Considering that the ins and outs of food allergy are difficult for the busy non-allergic MD to remember and that the literature is about as diffuse as the symptoms, I took pity on my fellow physicians, not to mention my patients, and stuck everything I could find on the subject in my office between two covers, and called it *Coping with Food Allergy*.

When should food allergy be considered as possibly etiologic in regard to an adult patient's symptomatology? Since allergy to food can affect any body system and mimic a variety of symptoms ranging from appendicitis to schizophrenia, it should be considered a distinct possibility when differential diagnosis has ruled out more serious contingencies. Especially it must be considered when there is a family history of allergy and when the patient suffers or has suffered other allergies, such as hay fever or colic, as an infant. Physicians beware! Be not quick to decide that yours is a neurotic or hypochondriacal patient. He may simply be allergic to his daily bread!

What constitutes a basic elimination diet and how does one vary it for an individual patient? Elimination diets must be tailored to individual patients—growing children, sedentary office workers, hard laboring men, etc. Basically, potent allergenic foods such as milk, eggs, wheat, chocolate, nuts, fish and shellfish, berries, peas, citrus fruits and corn are re-

moved, plus foods we can suspect from the patient's history, (or the patient does, since he often knows what doesn't agree) plus foods that appear positive in skin and challenge tests, although the former remain doubtful. Most importantly, vitamin and mineral deficiencies in such a diet must be made up by prescription lest we sink the ship trying to save it.

A physician called me about a patient who developed urticaria after eating mangoes. He later ate cashew nuts, followed by a severe reaction, and still later incurred a more severe reaction by eating pistachio nuts. What about an elimination diet here? The only foods that needed to be eliminated here were mangoes, cashew nuts and pistachio nuts. They are the only foods in the Cashew family. If a person is allergic to one food in a botanical family he should eliminate all foods in that particular family.

I have seen several patients severely allergic to peanuts. These patients had been seen by physicians—one by an allergist—and told to eliminate nuts. Peanuts belong to the legume family. These people were continuing to have symptoms as they continued to eat foods in this family. Foods in the legume family should have been eliminated, some of which are acorn, urticaria, kidney bean, green bean, lima bean, navy bean, soy bean, wax bean, licorice, black-eyed pea, chick pea, green pea, split pea and tamarind.

I always hand a copy of my book to the patient and tell him to read all about the food to which he is allergic, where it is found and its relationship to other foods.

What is the current status of skin testing to determine food allergy? Skin testing for food allergy is nowhere near as reliable as it is for inhalants, but I use such procedures on occasion, depending upon the patient and his history. Sometimes correlating skin test results with the history can provide helpful hints of where to go.

What is the current status of desensitization as treatment for food allergy? I find desensitization results as treatment for food allergy unconvincing and I do not use this procedure except for inhalants and insect stings.

### Eubie Blake, at 92, Gives 'Thank You' Concert



Jazz pianist Eubie Blake, 92, was recently admitted to Long Island College Hospital, Brooklyn, for a series of tests. After being pronounced in good health by his physician, Dr. George Liberman, he offered to give a concert for the hospital's staff and ambulatory patients before going home. Steadway Piano Company tuned the piano in the nurses' residence and the concert was on.

### What is the role of food additives as allergens?

I agree with Dr. Stephen Lockey that intentional and unintentional (pesticide residues, drug traces, etc.) additives pose an increasing health threat to the allergic. Allergists have already documented cases of patients reacting to such things as butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT), sodium nitrite, the salicylates and their derivatives, blood-clotting chemicals and chlorine, but there is a great deal we do not yet know about these thousands of chemicals added to our daily fare, including their synergistic effects and whether or not some of them are capable of sensitizing a good part of the population. Let us admit that we are ignorant and act accordingly.

### Next In Consultation

Dr. C. J. MARTIN, Director, Institute of Respiratory Physiology, Virginia Mason Research Center, Seattle, Wash., will discuss what's new and old important in the diagnosis of diffuse obstructive pulmonary syndromes and the mechanisms involved in causing these syndromes. He will also discuss the relationship between chronic bronchitis, emphysema and tuberculosis as well as the clinical significance of differential aeration and the emptying of different lung compartments. Dr. Martin will also discuss measures that may aid in preventing or arresting the progress of emphysema and pulmonary failure.

## Double Form of Gastrin Said To Flaw Radioimmunoassay

Medical Tribune World Service

MEXICO CITY—The usual radioimmunoassay technique of measuring peptide hormones in blood may not be providing an accurate index of their biological activity, the Fifth World Congress of Gastroenterology was told.

The statement was made by Dr. M. I. Grossman, Professor of Medicine, University of California at Los Angeles, in commenting on his work and that of Dr. R. A. Gregory, Professor of Physiology at the University of Liverpool.

Dr. Gregory reported that he determined the true sequence of amino acids in big gastrin in its predominant form of gastrin in blood, and found it has a chain of 34 amino acids, compared with 17 in little gastrin, which predominates in antral tissue. He explained the predominance of big gastrin in blood as due principally to its slower rate of removal.

Dr. Grossman said that he was able to demonstrate the same relationship between the two forms of gastrin in the blood and in the tumor tissue of patients with such disorders as Zollinger-Ellison syndrome.

In commenting on these findings, Dr. Grossman said:

"Actually, a general principle has been discovered. It is that peptide hormones occur in blood and tissue in more than one molecular form and the larger form can be transformed into the smaller form.

"Because of this heterogeneity, and because different forms have different activity, the measurement of the total amount of hormone is not necessarily a valid index of the biological activity of that hormone."

Dr. Grossman also observed that Dr. Gregory's finding has led to a new concept with respect to the relative potency of the two forms of gastrin:

"Equivalent amounts of big and little gastrin will produce about the same gastric response. Therefore, based on exogenous doses of hormone, the two forms are about equally potent on a molar basis. However, since the larger form produces a much higher blood level than the smaller one, the 'endogenous potency'—that is, the blood level required to produce a given response—is much greater for little gastrin."



# Exceptionally well absorbed oral broad spectrum antibiotic may be taken with meals

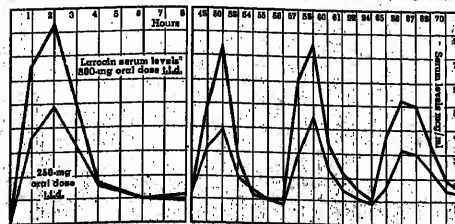
## Larocin (amoxicillin) achieves high blood and urine levels

### Low incidence of diarrhea to date in clinical studies

NUTLEY, N.J. — Roche Laboratories recently introduced an oral broad spectrum antibiotic: Larocin (amoxicillin). Larocin represents a significant contribution to antibacterial chemotherapy, one which will perform effectively in the treatment of a wide range of infections due to susceptible organisms (see chart at right).

#### Absorption called the key

The key pharmacologic characteristic of Larocin (amoxicillin) is its rapid and efficient absorption from the gastrointestinal tract. Not only is it stable in stomach acid, but the presence of food has no significant effect on the antibiotic's absorption. Thus Larocin may be taken by patients on a convenient t.i.d. schedule without regard to meals. The reconstituted oral suspension and pediatric drops may be added to liquid such as formula, milk, fruit juice or soft drinks for easy administration to small children. Because of its efficient absorption characteristics, high blood and urine levels of Larocin (amoxicillin) are rapidly achieved. Peak serum levels average 4.2 mcg/ml two hours after a single 250-mg oral dose and 7.6 mcg/ml one hour after a single 500-mg oral dose — both levels approximately twice as high as those obtained with equal doses of ampicillin.<sup>1,2</sup>



On a multiple-dose regimen, when given every eight hours for 8 days, the lowest mean serum levels of Larocin approximated 1.0 mcg/ml after 200 mg and 1.25 mcg/ml after 500 mg.<sup>3</sup> Although the therapeutic range of blood levels for the penicillins is not well established, these results demonstrate that blood levels may be expected to remain above the MIC's for all of the nonurinary pathogens susceptible to Larocin when it is administered at clinically recommended doses (see chart below).

Most of Larocin is excreted unchanged in the urine.<sup>4</sup> Average urinary excretion within 6 to 8 hours after oral administration ranges from 40 to 79% for the 250-mg dose and 59 to 76% for the 500-mg dose.<sup>5,6</sup>

L. Crocydon BAP, Sutherland R: *Antimicrob Agents Chemother* — 1970, pp. 467-480, 1971. 2. New HC, Winfield RJ: *Antimicrob Agents Chemother* — 1970, pp. 442-448, 1971. 3. Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey. 4. Lelch DA: *Curr Med Res Opin* 1:10-15, 1972. 5. Boddy GP, Nance J: *Antimicrob Agents Chemother* 1:358-362, 1973.

#### Hypersensitivity reactions can occur

As with other penicillins, it is anticipated that adverse reactions to Larocin (amoxicillin) will be largely limited to sensitivity phenomena. While anaphylaxis is rare in patients treated with oral

| GRAM-POSITIVE                            |  |
|--|--|
| Alpha-hemolytic streptococci             |  |
| Beta-hemolytic streptococci              |  |
| <i>Streptococcus faecalis</i>            |  |
| <i>Diphtheria pneumoniae</i>             |  |
| Nonpenicillinase-producing staphylococci |  |
| GRAM-NEGATIVE                            |  |
| <i>Haemophilus influenzae</i>            |  |
| <i>Escherichia coli</i>                  |  |
| <i>Proteus mirabilis</i>                 |  |
| <i>Neisseria gonorrhoeae</i>             |  |

**In vitro bactericidal activity**  
Note: Because Larocin (amoxicillin) does not resist destruction by penicillinases, it is not effective against penicillinase-producing bacteria such as resistant staphylococci. All strains of *Pseudomonas* and most strains of *Klebsiella* and *Enterobacter* are resistant.

penicillins, the possibility must nevertheless be kept in mind. Larocin is contraindicated in patients with a history of penicillin hypersensitivity. SERIOUS ANAPHYLACTOID REACTIONS REQUIRE IMMEDIATE EMERGENCY TREATMENT (See Warnings section of complete product information, a summary of which appears at right.)

#### Efficacy demonstrated in many infections

Amoxicillin has been administered successfully to patients with a wide range of commonly seen infections due to susceptible organisms.<sup>7</sup> Over-all clinical evaluation of Larocin therapy was considered a "success" or "improvement" in 1287 of 1850 evaluable cases (69.5%).<sup>8</sup>

Ages of the 1350 patients studied ranged from under one year to over 80 years. Larocin capsules were administered to 800 patients and oral suspension to the remaining 550. Doses of the capsules ranged from 250 mg t.i.d. (the most frequently used dosage) to a single 8-Gm dose for the treatment of acute uncomplicated gonorrhea. Dosage of the oral suspension ranged from 50 mg t.i.d. to 250 mg t.i.d., with 125 mg t.i.d. the most frequent. The majority of patients were treated from seven to 10 days. A breakdown by type of infection follows:

Otitis Media: The pathogens most commonly isolated were *Diplococcus pneumoniae* and *Haemophilus influenzae*. Of 200 cases with this diagnosis, 197 (98%) were rated as a "success" or "improvement" after treatment with Larocin (amoxicillin).

Streptococcal Sore Throat: A success rate of 86% (174 of 202 cases) was observed with Larocin against the responsible pathogen, beta-hemolytic streptococci.<sup>9</sup> The great majority of the 202 patients in this group were children who received the oral suspension.

Other Upper Respiratory Infections: Beta-hemolytic streptococci were the offending organisms for most of the infections in this group, which were diagnosed primarily as pharyngitis and some cases of tonsillitis and a few cases of sinusitis. A success rate of 82% (66 of 80 cases) was achieved with Larocin.

Lower Respiratory Infections: Treatment with Larocin resulted in a "success" or "improvement" in all of the 52 cases in which *Diplococcus pneumoniae* was cultured. *Staphylococcus aureus* was also cultured in 26 of the 88 cases; Larocin showed "success" or "improvement" in 95% (25 of 26 cases). The most common clinical conditions were bronchitis and bronchopneumonia.

Urinary Tract Infections: Cystitis, pyelonephritis and asymptomatic bacteriuria were the most frequent clinical diagnoses in this group. Of the 404 cases evaluated, *Escherichia coli* was cultured in 305 cases and treatment with Larocin resulted in "success" or "improvement" in 294 (96%). *Proteus mirabilis* was cultured in 70 patients, with Larocin effective in 67 (96%).

Skin and Soft Tissue Infections: *Staphylococcus aureus* was cultured in 108 cases, with "success" or "improvement" in 104 (96%); while beta-hemolytic streptococci were cultured in 90 cases, with "success" in 97 (98%). Impetigo and abscess were the most frequent diagnoses.

Gonorrhea: Administered as a single 8-Gm oral dose, Larocin showed a success rate of 97% in both males (85 of 88 cases) and females (114 of 118 cases).

<sup>1</sup> Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey 07110. <sup>2</sup> "Success" or "improvement" determined by a combination of clinical and bacteriological criteria. In infections due to beta-hemolytic streptococci and *N. gonorrhoeae*, only "success" and "improvement" were included.

#### Low incidence of side effects reported to date

During the clinical investigations with amoxicillin, all cases treated were evaluated for side effects. No side effects or laboratory abnormalities which would be considered unusual for a penicillin derivative were reported by any of the investigators.

In 2688 total courses of therapy with amoxicillin therapy was discontinued in only 52 patients

### Drug-Related Side Effects Associated with Amoxicillin

Based upon 2688 courses of therapy: 1811 with the capsules and 847 with the oral suspension.

| SIDE EFFECT                        | CAPSULES |      | SUSPENSION |     |
|------------------------------------|----------|------|------------|-----|
|                                    | #        | %    | #          | %   |
| Diarrhea                           | 24       | 1.3  | 18         | 2.1 |
| Rash                               | 24       | 1.3  | 17         | 2.0 |
| Nausea                             | 7        | 0.3  | 2          | 0.1 |
| Urticaria                          | 9        | 0.4  | 2          | 0.2 |
| Headache                           | 7        | 0.3  |            |     |
| Nausea/Vomiting                    | 3        | 0.1  |            |     |
| Diarrhea/Nausea                    | 2        | 0.1  | 4          | 0.4 |
| Vomiting                           | 2        | 0.1  |            |     |
| Optic neuritis                     | 2        | 0.1  |            |     |
| Cutis                              | 2        | 0.1  |            |     |
| Nausea/Headache                    | 2        | 0.1  | 1          | 0.1 |
| Rash/Urticaria                     | 1        | 0.05 |            |     |
| Esophageal Spasm                   | 1        | 0.05 | 1          | 0.1 |
| Stomachache                        | 1        | 0.05 |            |     |
| Swelling                           | 1        | 0.05 |            |     |
| Overdose                           | 1        | 0.05 |            |     |
| Swelling/Numbness/Tingling/Itching | 1        | 0.05 |            |     |
| Over/Itching                       | 1        | 0.05 |            |     |
| Offtact Breathing                  | 1        | 0.05 |            |     |
| Mucus In Pharynx                   | 1        | 0.05 |            |     |
| Diarrhea/Urticaria                 | 1        | 0.05 | 4          | 0.4 |
| Diarrhea/Vomiting                  | 1        | 0.05 |            |     |
| Optic neuritis/Headache            | 1        | 0.05 |            |     |
| Conjunctivitis/Erythema            | 1        | 0.05 |            |     |
| GI Bleeding                        | 1        | 0.05 |            |     |
| Abdominal Cramps                   | 1        | 0.05 |            |     |
| Diarrhea/Rash                      | 1        | 0.05 | 1          | 0.1 |
| Rash/Urticaria/Vomiting            | 1        | 0.05 | 1          | 0.1 |
| Sore Tongue                        | 1        | 0.05 |            |     |
| Rash/Vomiting                      | 1        | 0.05 |            |     |
| TOTAL                              | 102      | 5.6  | 82         | 8.1 |

(1.9%) because of drug-related side effects. Laboratory abnormalities possibly related to amoxicillin occurred infrequently.

In these studies, there was a low incidence of diarrhea related to amoxicillin capsules — 1.7% or 30 of 1811 patients. Especially noteworthy was the low incidence of diarrhea reported with amoxicillin oral suspension — only 2.8% or 24 of 847 patients, significantly less ( $p < 0.05$ ) than the incidence of diarrhea with ampicillin oral suspension (5.3% or 15 of 282 patients).

In breaking down the over-all incidence of diarrhea by age group, it was found that the incidence of diarrhea was higher in the newborn and infant age groups than in older children, which is true of all antibiotics.

#### Usual Adult and Pediatric Dosages

| INDICATION  | STRAIN ISOLATED   | ADULT DOSAGE             | PEDIATRIC DOSAGE*   |
|---|---|--------------------------|---|
| Infections of the ear, nose, throat                                   | Streptococci, pneumococci, nonpenicillinase-producing staphylococci, <i>H. influenzae</i> | 250 mg t.i.d.            | Oral Suspension: 20 mg/kg/day in divided doses t.i.d.<br>Drops: Under 6 kg (13 lbs): 0.5 ml t.i.d.; 6-8 kg (13-18 lbs): 1 ml t.i.d. |
| Infections of the lower respiratory tract                             | Streptococci, pneumococci, nonpenicillinase-producing staphylococci, <i>H. influenzae</i> | 500 mg t.i.d.            | Oral Suspension: 40 mg/kg/day in divided doses t.i.d.<br>Drops: Under 6 kg (13 lbs): 1 ml t.i.d.; 6-8 kg (13-18 lbs): 2 ml t.i.d.   |
| Infections of the genitourinary tract                                 | <i>E. coli</i> , <i>Proteus mirabilis</i> , <i>Strep. faecalis</i>                        | 250 mg t.i.d.            | Oral Suspension: 20 mg/kg/day in divided doses t.i.d.<br>Drops: Under 6 kg (13 lbs): 0.5 ml t.i.d.; 6-8 kg (13-18 lbs): 1 ml t.i.d. |
| Infections of the skin and soft tissues                               | Streptococci, pneumococci, staphylococci and <i>E. coli</i>                               | 250 mg t.i.d.            | Oral Suspension: 20 mg/kg/day in divided doses t.i.d.<br>Drops: Under 6 kg (13 lbs): 0.5 ml t.i.d.; 6-8 kg (13-18 lbs): 1 ml t.i.d. |
| Severe infections, or infections caused by less susceptible organisms |   | 500 mg t.i.d.            | Oral Suspension: 40 mg/kg/day in divided doses t.i.d.   |
| Gonorrhea, acute uncomplicated  | <i>N. gonorrhoeae</i>   | 3 grams—single oral dose |   |

\*Note: Children weighing more than 8 kg (18 lbs) should receive the appropriate dose of the Oral Suspension: 125 mg or 250 mg/5 ml. Children weighing more than 20 kg should be dosed according to adult recommendations.

Before prescribing, please consult complete product information, a summary of which follows:

**Indications:** Infections due to susceptible strains of the following gram-negative organisms: *Haemophilus*, *E. coli*, *P. mirabilis* and *N. gonorrhoeae*; and gram-positive organisms: streptococci (including *Streptococcus faecalis*), *D. pneumoniae* and nonpenicillinase-producing staphylococci. Therapy may be initiated prior to obtaining results from bacteriological and susceptibility studies to determine causative organisms and susceptibility to amoxicillin.

**Contraindications:** In individuals with history of allergic reaction to penicillins.

**WARNINGS: SERIOUS AND OCCASIONALLY FATAL HYPERSENSITIVITY (ANAPHYLACTOID) REACTIONS** REPORTED IN PATIENTS ON PENICILLIN THERAPY. ALTHOUGH MORE FREQUENT FOLLOWING PARENTERAL THAN ORAL THERAPY, ANAPHYLAXIS HAS OCCURRED IN PATIENTS ON ORAL PENICILLINS. MORTALITY IN INDIVIDUALS WITH HISTORY OF SENSITIVITY TO MULTIPLE ALLERGENS BEFORE THERAPY. INQUIRY INTO PREVIOUS HYPERSENSITIVITY REACTIONS TO PENICILLINS, CEPHALOSPORINS OR OTHER ALLERGENS. IF ALLERGIC REACTION OCCURS, INSTITUTE APPROPRIATE THERAPY AND CONSIDER DISCONTINUANCE OF AMOXICILLIN. SERIOUS ANAPHYLACTOID REACTIONS REQUIRE IMMEDIATE EMERGENCY TREATMENT WITH EPINEPHRINE, ADMINISTER OXYGEN, INTRAVENOUS STEROIDS AND AIRWAY MANAGEMENT, INCLUDING INTUBATION, AS INDICATED.

**Usage in Pregnancy:** Safety in pregnancy not established.

**Precautions:** As with any potent drug, a careful renal, hepatic and hematopoietic function periodically during prolonged therapy. Keep in mind possibility of superinfections with mycotic or bacterial pathogens; if they occur, discontinue drug and/or institute appropriate therapy.

**Adverse Reactions:** As with other penicillins, untoward reactions will likely be essentially limited to sensitivity phenomena and more likely occur in individuals previously demonstrating penicillin hypersensitivity and those with history of allergy, asthma, hay fever or urticaria. Adverse reactions reported as associated with use of penicillins: *Gastrointestinal:* Nausea, vomiting, diarrhea. *Hypersensitivity:* Erythema, maculopapular rashes, urticaria. *NOTE:* Urticaria, other skin rashes and

serum sickness-like reactions may be controlled with antihistamines and, if necessary, systemic corticosteroids. Discontinue amoxicillin unless contraindication believed to be life-threatening and amenable only to amoxicillin therapy. *Liver:* Moderate rise in SGOT noted, but significance unknown. *Hemic and Lymphatic Systems:* Anemia, thrombocytopenia, leukopenia, eosinophilia, leukopenia, agranulocytosis. All are usually reversible on discontinuation of therapy and believed to be hypersensitivity phenomena.

**Dosage:** *Ear, nose, throat, gonorrhea:* 3 grams, single oral dose. *Other infections—Adults:* 250 mg every 8 hours. Children: 20 mg/kg/day in divided doses every 8 hours; under 6 kg, 0.5 ml of Pediatric Drops every 8 hours; 6-8 kg, 1 ml of Pediatric Drops every 8 hours. *Lower respiratory tract infections and severe infections or those caused by less susceptible organisms—Adults:* 500 mg every 8 hours. Children: 40 mg/kg/day in divided doses every 8 hours; under 6 kg, 1 ml of Pediatric Drops every 8 hours; 6-8 kg, 2 ml of Pediatric Drops every 8 hours. *Gonorrhea* (acute uncomplicated aural and urethral infections)—Males and females: 3 grams as a single oral dose. *NOTE:* Children weighing more than 8 kg should receive appropriate dose of oral suspension 125 mg or 250 mg/5 ml. Children weighing 20 kg or more should be dosed according to adult recommendations.

**Note:** In gonorrhea with suspected lesion of apophysis, perform dark-field examination before amoxicillin therapy and monthly serological tests for at least four months. In chronic urinary tract infections, frequent bacteriological and clinical appraisals are necessary. Smaller than recommended doses should not be used. In stubborn infections, several weeks' therapy may be required. Except for gonorrhea, continue treatment for a minimum of 48-72 hours after patient is asymptomatic or bacterial eradication is demonstrated. Treat hemolytic streptococcal infections for at least 10 days to prevent acute rheumatic fever or glomerulonephritis.

**Supplied:** Amoxicillin as the trihydrate: Capsules, 250 mg and 500 mg; oral suspension, 125 mg/5 ml and 250 mg/5 ml; pediatric drops, 50 mg/ml.

**Larocin (amoxicillin)**  
an important contribution to oral broad spectrum antibiotic therapy. **ROCHE**

## Most Doctors Seen Failing In Dealings With Alcoholics

By JIM F. HENAHAN  
Special Tribune Correspondent

LOS ANGELES—Most physicians are either poorly equipped or reluctant to diagnose and treat alcoholism when they encounter it in patients or in their profession.

That indictment surfaced in various forms at a symposium—held during the California Medical Association's 14th annual session in Los Angeles—devoted to "Alcoholism and Other Drug Dependencies: The Physician's Responsibility."

"Even though physicians may have a common knowledge of the things in their patients' history that may be connected with alcoholism, they hesitate to make the diagnosis and usually wait until the patient goes into the withdrawal syndrome before they do," said Dr. Jude Hayes, medical director of the Tulare County Substance Abuse Program in California.

### Strong Clues Noted

Noting that fatty liver, hepatitis, chronic gastritis and a high blood alcohol level, along with a history of marital and job disorders, accidents and other behavioral upsets are strong clues to alcoholism, Dr. Hayes observed that "the physician feels that he just doesn't have the time or counseling skills to deal with an alcoholic patient."

"It is very important that the physician maintains a close and understanding relationship with the alcoholic patient," he urged.

"If it will accomplish nothing else, it will give the patient the realization that he still belongs to the community and that he has not been abandoned to some quasi-governmental agency for treatment."

A physician's reluctance to diagnose and work with the alcoholic patient may also be due to the fact that after he has had some success, the patient frequently goes back to drinking as heavily as ever before.

"The physician then feels that he is somehow responsible for the failure and overlooks the fact that recurrence is the nature of the disease, just as it is in chronic rheumatic disease, coronary artery disease, and cancer," Dr. Hayes said.

### Blood Level Data Persuasive

Although it is usually difficult to get the patient to acknowledge that he is an alcoholic, Dr. Hayes believes that the initial step could be taken by confronting the patient with a blood level in the range of 150 mg. per 100 ml. It should be made clear to the patient, he suggested, that even though he does not appear intoxicated at the moment, the blood level is a strong indication that he is an alcoholic and needs help.

"Now that the treatment of alcoholism is being funded by insurance carriers, and a growing number of employers and government agencies now view alcohol as a disease, and not merely a bad habit, the physician is in a better position than ever before to carry out his responsibility to the alcoholic patient," Dr. Hayes said.

Dr. William Lukasch, White House

Physician, told a luncheon meeting of the C.M.A. that young doctors are still not receiving enough education in the management of alcoholism.

He suggested that the fact that only 20 percent of all those now enrolled in Alcoholics Anonymous are there through physician referral, indicates that "we still have a long way to go in this area."

While diagnosis of alcoholism usually associated with some other illness may appear in a patient's record, few are being treated for it, according to Dr. Charles Becker, Head of the Division of Clinical Pharmacology at San Francisco General Hospital.

He cited two surveys taken at San Francisco General over the last several months which indicate that although a group of patients with pancreatitis were diagnosed as alcoholics, the number referred for treatment of alcoholism was "virtually zero."

"In addition," he said, "although the pancreatitis was treated correctly, by failing to consider the alcoholism problem, the physician did nothing to prevent its recurrence. This is clearly a severe deficit in health care delivery."

Dr. Becker said that his technique for treating alcoholics is to use sedatives to detoxify the patient as soon as symptoms of alcoholism are recognizable. Then while the patient is coming back to normal, he administers Antabuse, to keep him away from alcohol during the recovery period.

"The advantage of this type of treatment is that it gives the physician time to build the proper patient-physician relationship. Then when you have the patient free of alcohol, he should be in a state of mind where you can employ Alcoholics Anonymous, group therapy, individual therapy or just plain human concern."

### Special Training Not Needed

"I don't agree that you have to be specially trained to give the proper alcoholic counseling. When a physician says he doesn't have time for the alcoholic, he really means that he doesn't have time to deal with the human aspects of treatment, and when medical practice gets that way, the physician is not rendering overall care to the patient."

If the physician has trouble confronting his alcoholic patients, he may even have more difficulty confronting and admitting his own drinking problems, said Dr. Max A. Schneider, medical director of the Beverly Manor Hospital in Orange, Calif.

For example, he said, it could reduce his objectivity in diagnosing alcoholism in his patients.

"Certainly I am a man before me for whom I'm taking a history is drinking a pint a day and I'm drinking a quart a day. I am not going to be very interested in his alcohol problem. Obviously he couldn't have one, because if he has one, I have one."

"As it is with the general patient, silence is the worst treatment for the alcoholic physician," Dr. Schneider told the C.M.A. symposium, adding that in the case of alcoholic physicians, ignoring a colleague's disease can pose

## Now It's 'Cricket' for the Blind to Bicycle



Device called "Cricket," from the sound it emits, invented by a Western Electric engineer, permits a blind person to enjoy bike riding on safe roads or trails. He rides his bike behind another equipped with a "Cricket" (extending from behind the leader's seat). The beep's pitch can be altered so that the blind rider can follow safely from as far as 200 feet or as close as a few feet.

serious safety for himself, his patients, his family and the entire profession.

As an aid to the alcoholic physician Dr. Schneider recommended that every hospital should set up a committee to whom anyone on the staff could submit a report indicating that a physician's drinking was getting in the way of his practice. And when the committee acts, its prime motivation should be therapeutic and not disciplinary, he said.

Dr. Schneider also suggested that local medical societies might follow the "Physician's Hot Line" approach that the Orange County Medical Society has been operating successfully for the last two years. The Hot Line number is known only to physicians and their families and all calls are completely confidential.

"In this way we can refer the alcoholic physician to other physicians who are ready and willing to listen to him and to assist him. At the same time, the process of 'role interruption' is immediately set in motion."

### Hypnotism Curb Asked

Medical Tribune World Service

TET. APY.—The Israel Medical Association has again come out strongly in favor of allowing only licensed physicians to practice hypnotism, following a case in which a stage hypnotist put a 16-year-old girl into a trance and was unable to wake her. The girl was roused nearly a week later by the head of the Israel Association for Medical Hypnotism.

## Behavior Modification a 'Lightning-Rod Issue'

Medical Tribune Report

DALLAS—Behavior modification is a "lightning-rod issue" in mental health, Dr. Bertram Brown, Director of the National Institute of Mental Health, said here.

"Drawn to behavior modification therapy," Dr. Brown said, "are such highly charged issues as fears of mind control and concerns about the treatment of persons institutionalized against their will."

He attributed a portion of the present ethical controversy of behavior modification to its overpopularization in such works as the movie "Clockwork Orange," and to an "incorrect linkage" to other psychiatric techniques such as psychosurgery and chemotherapy.

Dr. Brown spoke to a Symposium on Human Experimentation presented by Southern Methodist University School of Law.

Apart from the obvious misconceptions about behavior modification therapy, he said, there are serious and responsible reasons for some concern about its legal and ethical aspects.

The most frequently criticized use of behavior modification, he noted, is its use in altering the behavior of persons who are involuntary participants in therapy.

"The mental health worker who proposes to modify the patient's environment to alter maladaptive behavior can be seen as serving the interests of the institution rather than favoring the right of the person to express his individuality," he said.

"Behavior modification is not a one way method that can be successfully imposed on an unwilling individual," he said. "By its nature, behavior modification will succeed only when the individual is responsive to the therapist and cooperates with treatment programs."

### Problems Vary With Settings

Dr. Brown contended that one difficulty in establishing ethical standards for behavior modification is that the problems vary with different settings. In prison, where the behavioral professional is in the position of assisting in the management of rebellious prisoners, he remarked, the distinctions among therapy, management, and rehabilitation may become blurred.

"Informed consent is clearly meaningful when a normal adult voluntarily seeks such treatment in an out-patient clinic," he said. "With prisoners it is a different matter, and it by no means clear that they are even able to give truly voluntary consent. There are special pressures to participate..."

A further evaluation must also be made of informed consent in relation to the child in the mental retardation school, Dr. Brown noted. "What about the mentally retarded child that continuously bangs his head, yet can't give informed consent?" he asked. "There are certain types of behavior modification that could possibly turn him into

A common position at present, he said, is to recommend the elimination of behavior modification programs in prisons, on the grounds that such therapy is coercive. "Yet if constructive programs are eliminated, the opportunity for inmates who genuinely want to participate and who might benefit is denied."

### The Mentally Retarded Child

A further evaluation must also be made of informed consent in relation to the child in the mental retardation school, Dr. Brown noted. "What about the mentally retarded child that continuously bangs his head, yet can't give informed consent?" he asked. "There are certain types of behavior modification that could possibly turn him into

a more adapted child but who gives persuasion? the parents, therapists, who?"

Dr. Brown advised therapists to first evaluate the extent to which the target population can truly give consent, then for the therapist and patient to weigh through a review committee the benefits against the possible risks of treatment.

"This is still a new form of therapy," he said. "It has been fully developed only in the last five years and it is basically built on a foundation of human experimentation."

"Particularly strong is the need for additional research comparing the efficacy of behavior modification methods with that of alternative treatment approaches," he said.



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In this age of synthetics  
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**Senokot** tablets  
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Natural senna from the *Cassia acutifolia* plant has been used as a laxative for over 3000 years. Purified and standardized for uniform action in SENOKOT preparations, it offers virtually colon-specific, gentle, predictable overnight laxation...virtually free of side effects when given at proper dosage levels.

Art's conception of a *Cassia acutifolia* plant.

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### Myasthenia Gravis Booklet

Medical Tribune Report

NEW YORK—A nine-page "fact book" on myasthenia gravis has been published by the Greater New York Chapter of the Myasthenia Gravis Foundation. The booklet is intended for patients and the public.

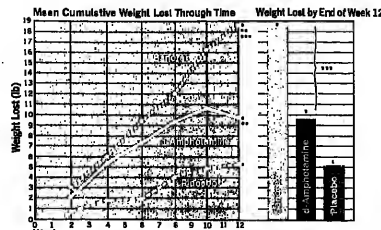




the soft underbelly of American health

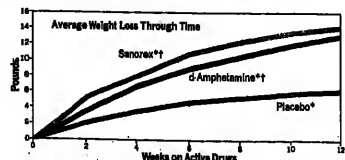
TABLETS, 1 mg and 2 mg.

## AS EFFECTIVE AS d-AMPHETAMINE



In a double-blind study of 40 obese patients (all of whom completed the study), Sanorex (1 mg t.i.d.) was more effective than either placebo or d-amphetamine (5 mg t.i.d.) in helping patients lose weight.

The 14 patients on Sanorex experienced a substantially greater mean weight loss—125 to 130 lb/wk, as compared with 1 to 12 lb/wk for the 14 d-amphetamine patients—throughout the 12-week phase of active medication. After the sixth week, the superiority of Sanorex became increasingly evident. And as treatment progressed, so did weight loss in patients on Sanorex—whereas after the tenth week, patients on d-amphetamine began to regain some weight.



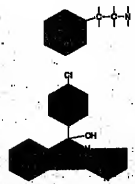
In a double-blind study of 93 obese patients (all of whom completed the study), 30 patients received Sanorex (1 mg t.i.d.), 31 received placebo, and 32 received d-amphetamine (5 mg t.i.d.).

During the 12-week phase of active medication, patients on Sanorex lost an average of 14.1 lb, compared with 13.1 lb for d-amphetamine patients and 5.5 lb for placebo patients. Throughout the active medication phase, 63% of patients on Sanorex lost more than 1 lb/wk, compared with 38% of the d-amphetamine group and 29% of the placebo group.

## BUT WITH CERTAIN DIFFERENCES

Although the pharmacologic activity of Sanorex and that of amphetamines are similar in many ways (including central nervous system stimulation in humans and animals, as well as production

### Different Chemical Structure



An important chemical similarity between amphetamines and all other prescription anorexics except Sanorex is the basic phenethylamine structure to which their differentiating chemical radicals are attached.

An important chemical difference between Sanorex and all other prescription anorexics is that Sanorex is an imidazole; it does not contain a phenethylamine structure.

of stereotyped behavior in animals), animal experiments suggest that there are differences.\* Sanorex also differs in basic chemical structure from amphetamines and all other prescription anorexics.

### Different Neurochemical Action

**Action of d-Amphetamine** In animal studies, d-amphetamine (like intake of food) activates efferent neurons leading to appetite centers in the hypothalamus. Resulting release of norepinephrine activates the receptor neurons. Unlike food, however, d-amphetamine also suppresses norepinephrine synthesis. Thus, increasingly larger doses of d-amphetamine become necessary to produce an effect.

**Action of Sanorex (mazindol)** After intake of food stimulates the release of norepinephrine from the afferent neuron, Sanorex blocks its reuptake without disturbing normal synthesis and release.

\*The significance of these differences for humans is uncertain.

### Simplicity and Flexibility of Dosage

Simple one-a-day dosage is facilitated by 2-mg tablets (taken 1 hour before lunch).

New flexibility (for the patient in whom 1 mg t.i.d. is preferred) is now facilitated by new 1-mg tablets (taken 1 hour before meals).

For Brief Summary, please see facing page.

Wednesday, April 23, 1975

## SANOREX® (MAZINDOL)®

Reference  
1. Kornblau A. Problems and current concepts in the treatment of obesity. Scientific Exhibit presented at the New York State Academy of Family Physicians, 25th Annual Scientific Convention, Syracuse, NY, May 8-10, 1975.  
2. Delfino J. Clinical evaluation of mazindol, dextroamphetamine, and placebo in treatment of obese patients. Curr Ther Res 15:359-366, July 1973.  
3. Varnier BJ. Practical considerations for managing obese patients. Interview and effective treatment in the office. Scientific Exhibit presented at the American Medical Association, 178th Clinical Convention, Anaheim, Calif, Dec 1-4, 1973.

Indicated in exogenous obesity, as a short-term (a few weeks) adjunct in a weight reduction regimen based on exercise and diet. The limited usefulness of agents of this class should be measured against possible risk factors. Contraindications: Glaucoma; hypersensitivity or idiosyncrasy to the drug; agitated states; history of drug abuse; during, or within 14 days following, administration of monoamine oxidase inhibitors (hypertensive crisis may result).

Warnings: Tolerance to many anorectic drugs may develop within a few weeks. If this occurs, do not exceed recommended dose, but discontinue drug. May impair ability to engage in potentially hazardous activities, such as operating machinery or driving a motor vehicle, and patient should be cautioned accordingly.

Drug Dependence: Mazindol shares important pharmacologic properties with amphetamines and related stimulant drugs that have been extensively abused and can produce tolerance and adverse psychological dependence. Manifestations of chronic overdose or withdrawal with mazindol have not been determined in humans. Abuse of the drug has been observed in dogs after abrupt cessation for prolonged periods. There was some abuse of the drug in the drug in monkeys. EEG studies and "liking" scores in human subjects yielded equivocal results. While the abuse potential of mazindol has not been further defined, possibility of dependence should be kept in mind when evaluating the desirability of including the drug in a weight-reduction program.

Use in Pregnancy: In rats and rabbits an increase in neonatal mortality and a possible increased incidence of rib anomalies in rats were observed at relatively high doses. Although these studies have not indicated important adverse effects, the use of mazindol in pregnancy or in women who may become pregnant requires that potential benefit be weighed against possible hazard to mother and infant.

Use in Children: Not recommended for use in children under 12 years of age. Precautions: Insulin requirements in diabetes mellitus may be altered. Small amounts of mazindol feasible should be prescribed or dispensed at one time to minimize possibility of overdose. Use cautiously in hypertension, with monitoring of blood pressure; not recommended in severe hypertension or in symptomatic cardiovascular disease including arrhythmias.

Adverse Reactions: Most commonly, dry mouth, tachycardia, constipation, nervousness, and insomnia. Cardiovascular: Palpitation, tachycardia, Central Nervous System: Overstimulation, restlessness, dizziness, insomnia, dysphoria, tremor, headache, depression, nervousness, weakness. Gastrointestinal: Dryness of mouth, unpleasant taste, diarrhea, constipation, nausea, other gastrointestinal disturbances. Skin: Rash, excessive sweating, clamminess. Endocrine: Impotence, changes in libido have rarely been observed. Eye: Long-term treatment with high doses in dogs resulted in some corneal opacities, reversible on cessation of medication; no such effect has been observed in humans.

Dosage and Administration: 1 mg three times daily, one hour before meals, or 2 mg once daily, taken one hour before lunch.

How Supplied: Tablets, 1 mg and 2 mg, in packages of 100.

Indicated Prescribing or Administration: See package circular for Prescribing Information.

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## Congenital CMV Infections Linked to Low IQ, Deafness

Continued from page 1

Medicine and sponsored by the National Foundation-March of Dimes.

Describing the findings on intelligence levels, the investigator explained that 10 levels of the positive children were compared with those of two other groups: an equal number of controls matched for age, sex, race, birth weight, and social class (Hollingshead classification); and 44 children born immediately after the birth of an infant with CMV-IgM antibody in the cord serum.

All told, 20 of the children had an IQ below 90. Dr. Hershov said. Of this number, 12 were in the CMV-IgM positive group while only six came from the matched control group and two from the random controls.

Of the seven children who had an IQ below 80, all had been CMV-IgM positive at birth.

Abnormalities in 16 of 44

Dr. Hershov noted that 16 of the 44 positive children (36.3 per cent) showed intellectual, behavioral, neurological, or sensory abnormalities "sufficient to predict the need for special education not available in the usual school setting."

By contrast, school failure was predicted in six of the matched controls and two of the random-control children.

Bilateral hearing loss was found in five of the positive group, the investigator said, and three of these children are profoundly deaf. Only one child in each of the control groups had bilateral loss.

The effect of social class on congenital CMV infection was evident, Dr. Hershov commented. Although the majority of the more than 8,000 infants tested were from middle-class families, CMV-IgM antibody was found twice as often among infants born to parents in the lower socioeconomic groups.

Also, all 16 of the antibody-positive children with abnormalities "precluding adequate performance" in a normal school setting came from the lower socioeconomic groups. But this finding, in Dr. Hershov's view, does not rule out the possibility that congenital CMV infection may diminish the intellectual potential of children from middle and upper socioeconomic groups.

### Available Drugs Toxic

In a second report on CMV, Dr. David J. Lung, of Duke University Medical Center, labelled it "the infectious agent most frequently associated with congenital injury, and damage" and cautioned that chemotherapy of such infections "has been disappointing thus far."

Dr. Lung cited present estimates that about 40 to 50 per cent of white, middle-class women in this country are CMV antibody positive by the time they reach childbearing age, while higher rates of antibody prevalence— and earlier acquisition of infection— have been reported among blacks and people of low socioeconomic status. Approximately one per cent of all live-born infants are congenitally infected

and at least 10 per cent of these eventually manifest significant damage.

The drugs now licensed for experimental trials in man are associated with significant toxicity, the investigator said. As a result, he believes it is not likely "in the foreseeable future" that a prospective therapeutic agent will be available among congenitally infected infants who seem reasonably healthy.

A further problem cited by Dr. Lung is the difficulty of making a clinical identification of a primary CMV infection during pregnancy. It appears most often as a mild, undifferentiated or subclinical illness, he pointed out, and the clinical syndromes "are even less well defined than those accompanying rubella."

Although Dr. Lung agrees that a CMV vaccine is needed, he warned that many questions must be resolved before more clinical trials of the present experimental vaccine could be justified.

There is no precedent for the "deliberate administration of a virus that may establish a latent or persistent infection," he said. Additionally, there are no criteria established for attenuation of CMV—and these are hard to determine "when the wild-type virus usually induces very mild illnesses."

Other questions posed by Dr. Lung: Is the apparent attenuation achieved after tissue culture passage liable to in-

### Computer Placement



Minnesota communities affected by shortages of medical personnel, many in isolated areas near the Canadian border, are being helped by a computer placement service of the University of Minnesota. The service matches economic base, recreational facilities, and population of towns with the preferences of graduating medical students. Above, a third-year student looks over the list of communities wanting a doctor.

crease the likelihood of the persistence of CMV and/or the neoplastic transformation of infected cells? Would n "killed virus" vaccine interrupt patterns of CMV transmission?

"In spite of the pressing need for control of CMV," he concluded, "insufficient information exists relevant to natural patterns of virus spread and control to permit the evaluation in man of modified CMV strains at this time."

## Beneficial Results Reported With Splenic Artery Ligation

By RALPH COBHAM  
Special Tribune Correspondent

TUCSON, ARIZ.—A University of Arizona surgeon has revived a 95-year-old procedure to reduce the need for—and risk of—splenectomy in hypersplenic patients.

Dr. Charles L. Witte, of the University of Arizona College of Medicine, told the annual meeting of the Society of University Surgeons that he has obtained beneficial results with splenic artery ligation in selected patients with hypersplenism, certain blood dyscrasias, and cirrhosis of the liver.

Dr. Witte said the advantage of splenic artery ligation is that it reduces the activity of the spleen without total destruction of the organ.

Noting that total splenectomy increases the risk of infection, he said it has not yet been demonstrated that the spleen's protective function is retained after splenic artery ligation, "but that is what we are trying to show."

Dr. Witte and co-workers are injecting rats with sheep erythrocytes, the antibody to which is produced in the spleen.

"Splenectomized rats will not produce the antibody," he said. "We are hoping that the ligated ones will."

In previous experiments, he went on, splenic artery ligation reversed hemolytic abnormalities in Sprague-Dawley rats in which hypersplenism had been artificially induced.

The procedure was then tried in twin boys with hereditary spherocytosis and

n young girl with idiopathic thrombocytopenic purpura (ITP).

"These patients had a reduction in their functional splenic mass," Dr. Witte reported, "and in the hereditary spherocytosis, the most important thing is that the blood hematocrit and reticulocyte count have been stable for almost 18 months."

### Immediate Rise in Platelets

"In the patient with ITP we had an immediate rise in platelet count, bounced around for a while, but 16 months postoperatively it was normal."

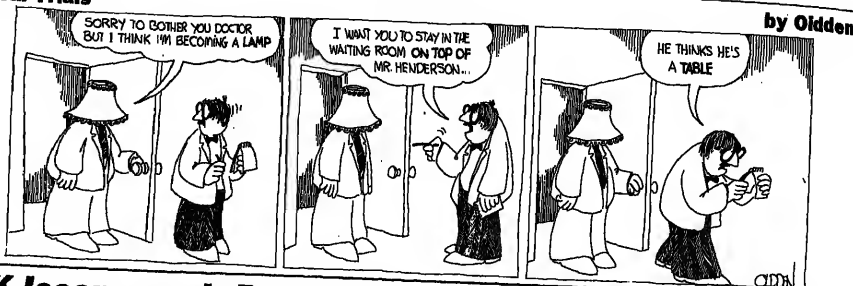
"One can get spontaneous remission in ITP," he said, "but the fact is this girl had symptoms of bruisability and nosebleeds and low platelet counts for a year before we ligated the artery."

Among the other patients were three with cirrhosis of the liver and splenomegaly with various kinds of cytopenia, Dr. Witte said.

Splenic artery ligation produced—in two of the patients—clinical, symptomatic, and blood count improvements, he said, adding that "it may not be as good as if we had done a splenectomy, but it's good enough to produce a remission and they still have the advantage of the splenic veins in that area."

"Putting the ligature too close to the origin of the splenic artery rather than at the end may be why earlier efforts with this procedure failed," Dr. Witte commented. "They may have been getting tremendous collaterals without even knowing it."

## Clinical Trials



## CPK Isoenzyme Is Reported Good Index of Size of Infarct

Continued from page 1

The studies of infarct size were made by a new kinetic fluorimetric procedure developed at the St. Louis center that can assay MB CPK quantitatively, according to Dr. Robert Roberts. Estimates were based on hourly changes in serum values of the isoenzyme.

With uncomplicated infarction, he commented, the isoenzyme released into serum paralleled total CPK release. Estimates of infarct size calculated from MB CPK and from total CPK agreed closely, with a correlation coefficient of 0.97.

### Complicated-Infarction Studies

Dr. Roberts said the special usefulness of the quantitative assay of MB became apparent in studies of patients with complicated infarction. In such cases, he said, realistic estimates of infarct size based on total CPK are not possible because noncardiac CPK will have been liberated into the circulation. It was found that infarct size esti-

mated from serial changes in the serum isoenzyme activity was significantly less than the size estimated from total CPK. The investigators conclude that the isoenzyme approach permits a reliable evaluation of the extent of infarction in patients with shock accompanied by release of CPK from sources besides the heart.

Describing assays of the isoenzyme following cardiac catheterization, Dr. Philip A. Ludbrook reported that blood samples for determination of total CPK and MB isoenzyme activity were obtained from 50 patients immediately before the procedure and every two hours thereafter for 24 hours.

None of these patients developed clinical or ECG evidence of myocardial injury or infarction.

For purposes of comparison, the same determinations were made on 50 patients with recent transmural myocardial infarction and on 20 hospitalized controls with no form of cardiac disease.

Total peak CPK activity was significantly elevated in three-fourths of the 50 patients undergoing catheterization and mildly increased in the rest, Dr. Ludbrook said.

"However, MB CPK activity remained within the normal range in all cases," he reported, "indicating that myocardial damage did not occur and that increased total CPK activity did not reflect release of enzyme from the heart."

In the 50 patients with documented myocardial infarction, peak total CPK activity was also significantly elevated—reaching levels considerably higher than those observed in the catheterization group. But in sharp contrast to the MB findings in cardiac catheterization patients, all 50 of the infarction patients showed significantly elevated MB CPK isoenzyme activity.

The CPK elevations seen after catheterization reflect release of enzyme from noncardiac sources rather than from injured myocardium, Dr. Ludbrook said. Increased serum MB CPK isoenzyme activity, he added, remains a specific and sensitive criterion of myocardial damage in patients undergoing cardiac catheterization and coronary angiography.

Consultants of the two reports included Drs. Burton H. Sobel and Edward S. Weiss, H. Dieter Ambror and Elaine M. Carlson.

## Chromatids Perform a 'Dance of Life'



Chromatids performing a "Dance of Life" as painted by Barbara Harris is one of a series of murals done by fine art students to brighten the otherwise drab facade surrounding the construction site of the Surgery-Brain Research Pavilion now going up at the University of Chicago.

## Survey Finds Little Change In Clinician Use of Rauwolfia

### Chronology of 3 Studies on Rauwolfia Therapy

The first studies to link rauwolfia therapy and breast cancer were done by interlocking groups at the Boston Collaborative Drug Surveillance Program, Oxford University, and the University of Helsinki (Lancet, Sept. 21, 1974.)

The next study, from the Chicago Peoples Gas Company (MT, December 25, 1974), found no evidence of a link between rauwolfia therapy—in men—and cancer, but indicated that there may be an association between hypertension and cancer.

Most recently (MT, April 9), a Mayo Clinic study, using women with cholelithiasis as controls, found no excess of breast cancer in women who had been on rauwolfia therapy. An H.E.W. ad hoc committee, meeting to assess these data at the National Heart and Lung Institute on March 24-25, called for more data and further examination.

relationship between reserpine and cancer.

What the whole matter suggests to him, Dr. Langford said, "is a cluster, or a constellation... or a syndrome, you might say, of being a little hypertensive, and a little obese, and going to the doctor, and getting drugs—and these could also go along with gallbladder disease."

He added that all his patients have been informed about the studies concerning rauwolfia derivatives and "practically none of them have asked to be taken off it."

Continued from page 1  
very muddy at the moment and I think it's going to take a lot of careful prospective looking-at with years of therapy."

"Breast cancer is very common in obese people and hypertension is very common in obese people. And hypertension is very common in the age group that gets breast cancer, around menopause. I think the only answers will come from prospective studies." Dr. Jeremiah Stamler of Northwestern University Medical School calls the situation "troublesome." "There is reason for concern," he said, "but I think at this point the issue is open."

### 'Situation Troublesome'

"I don't think one can conclude that a definite association [between rauwolfia use and cancer] has been demonstrated, or that a definite association has been refuted."

"I think the situation is troublesome because reserpine is a very useful drug. It's effective, and low cost, and many people have tremendous risks because of hypertension."

"Pending further evaluation, we're continuing to use the drug. We're watching closely, but we're continuing to use it," Dr. Stamler said.

Dr. Herbert G. Langford, Director of the University of Endocrinology and chairman of the steering committee of the National Hypertension Detection and

Follow-up Program, also said he feels more studies need to be done. On the basis of the studies so far, though, he said he would "bet against" a causal

## One Man...and Medicine

ARTHUR M. SACKLER, M.D.,  
International Publisher, Medical Tribune



### Mystification

Part I

FOR YEARS, as we sought to quantitate experimental stress utilizing simple stimuli such as sound and vibration, we noted marked physiologic deviations in our experimental animals. I therefore was upset to confront Lennard et al's pejorative "mystification" as a challenge to practicing physicians who use pharmacotherapy

believed I was promoting a good night's sleep, in a difficult environment, under trying circumstances.

### Belief about Drugs

The book advances the authors' belief that "The contemporary trend of increasing prescriptions of psychoactive drugs seems to be contributing to the requirement of more and more persons into a way of life in which the regulation of personal and interpersonal processes is accomplished through the ingestion of drugs."

There is no consistency, however, between the known pattern of illegal psychoactive drug abuse—highest in young males, and for hard drugs, highest in black males, and the authors' report that a national survey of prescription drug use in 1967 "found that more in many women (31 per cent) use (15 per cent) had used psychoactive agents during the preceding 12 month period.... There were also major differences in psychoactive drug use among religious and racial groups. The same survey found that Jews use psychoactive drugs considerably more than do Catholics or Protestants and that the percentage of Negroes using psychoactive drugs is only about one-half (13 per cent) that of whites (26 per cent)." Clearly there is no relationship either between the number of physicians practicing or prescribing in ghetto areas and heroin abuse; nor is the frequency of alcoholism higher in Jews than in Catholics or Protestants nor does the incidence of alcoholism relate to the sex differences in psychoactive prescriptions. In fact, these are 180 degrees out of phase.

### Addiction and Social Influence

Despite the indisputable fact that social influences do affect addiction, it must be recognized that the most frequent and most serious prototype of Western addiction, alcoholism, not only occurs across economic groups in any one society but affects even the most varied social structures. Alcoholism in capitalist Atlanta City does not distinguish itself readily from alcoholism in communist Zagreb; Leningrad does not have a lower incidence than London, or Warsaw than Washington. As to non-western psychotics, the use of charas in Calcutta doesn't differ in ultimate effects from marijuana in Marrakesh, gangs in Ghana, kif in Kashmir, or hashish in tribal areas of Africa.

Which social system has solved the

problem of psychoactive drug abuse? Apparently neither the tribal nor communist forms of society, nor the democratic, nor monarchical systems. It becomes imperative, therefore, to seek to isolate relevant elements with realistic potentials for prevention or control or reduction in abuse.

Next week "mystification" continues. Part II.

1. Science, 169:438, July 31, 1970  
2. Mystification and Drug Misuse, U. L. Lennard et al, Jossey-Bass, Inc., San Francisco, 1971.  
3.1. New & Mend, Dis 145:69, July, 1967

### EPICRAMS: Clinical and Otherwise

A sick man dreams nothing so dreadful that some philosopher isn't saying it.

Marcus Terentius Varro  
116-27 B.C.  
Satires, frag. 122

### Medicine on Stamps

Tablar



Born in 705, Jabir, or Geber, was a healer, though he is best known as the father of modern chemistry. He is credited with the discovery of nitric acid and aqua regia and described distillation, filtration, and sublimation. About 500 books have been attributed to his authorship.

Test: Dr. Joseph Kler  
Stamp: Minkus Publications, Inc., New York

## Doctor Resistance to PSROs Is Dying Out, Says Simmons

Continued from page 1

changed their positions—for example, Indiana, Illinois, Nebraska. I'm convinced that in virtually every area of the country, the profession will come forward and do the job, and there'll be no need to bring in non-physicians to organize the program."

According to Dr. Simmons, there are only four states (Georgia, Texas, Oklahoma and Louisiana) where no plans have yet been filed. The PSRO mandate of the 1972 Social Security amendments, designed to oversee hospital care of Medicaid and Medicare patients, curries a Jan. 1, 1976 deadline for submission by local physicians of acceptable plans of implementation to H.E.W. Failing this, medical schools or consumer groups might be brought in to tailor the program in place of physicians.

### Measuring Up to Expectations

Early data on operative PSROs indicates to Dr. Simmons that they are measuring up to expectations. He cited reports of decreased length of hospital stays from each of the districts. Less tangibly, he believes there has been an improvement in the quality of care provided in these districts. He revealed that several private insurers, among them the "Blues" and the Health Insurance Association of America, have expressed interest in having PSRO committees pass on their patients, and are now negotiating with H.E.W. to coordinate and unify review mechanisms.

"Eventually, I expect there will be a uniform system of reviewing all hospital patients, whether their bills are being picked up by the government or third-party private insurers, and irrespective of when or whether we get National Health Insurance. I don't rule out the possibility that one day outpatients will be covered, too. Some PSROs are already trying this experimentally."

Although he thinks PSRO will mesh smoothly with a National Health Insurance scheme, Dr. Simmons does not see NHF as a prerequisite to success.

### A 'Problem,' Not a 'Crisis'

Nevertheless, Dr. Simmons insisted on calling the budgetary matter a "problem" rather than a "crisis," and denied that it was endangering the survival of the program, as both some supporters and opponents of PSRO have implied.

He also sought to minimize the effect of the suit now being heard in federal court in Chicago, in which the A.M.A. is trying to block H.E.W. plans for hospital utilization committees that would include non-physicians. These committees, he said, would only be temporary and would be phased out as soon as PSROs were in place.

As for civilian participation, it was for the doctors' own good—"to relieve them of onerous paperwork. Contrary to what the A.M.A. says, all final decisions are still reserved for physicians."



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## Harvard Enters Pact on Cancer With Monsanto

Medical Tribune Report

BOSTON—The Harvard Medical School and the Monsanto Company are understood to have entered into a "working arrangement" under which the company will provide cancer research financing in return for the commercial rights to any resulting discoveries.

The funding, over 12 years, may reach a total of \$23,000,000, plus biological materials, equipment development, and industrial know-how, according to informed sources. The money is intended to support the work of two Harvard scientists, Drs. M. Judah Folkman and Bert L. Vallee, who have each made important discoveries in basic cancer research.

The school and the company described the arrangement as an alliance designed to permit the Harvard scientists to pursue their research wherever it may lead, without interference.

An independent advisory board will protect the rights of both parties and those of the public, it was reported.

### Toward Rapid Application

Framers of the agreement not only see mutual benefits, but also feel there is a need to develop a system of applying accumulating knowledge more rapidly to meet human needs. They expect this alliance to generate practical techniques for accomplishing this.

Dr. Folkman is chief of surgery at the Children's Hospital Medical Center here. He is best known perhaps for his work in growing whole malignant tumors to permit long-term studies on their growth rate and metabolism. He recently identified a tumor angiogenesis factor (TAF) that triggers the development of the blood vessels that feed such tumors.

Dr. Vallee's research has focused on the function of a zinc-dependent enzyme in the leukemic process that he hypothesized more than 25 years ago, long before tools for quantitating it existed. He is director of the medical school's Biophysics Research Laboratory at the Peter Bent Brigham hospital.

In the Harvard-Monsanto project, the two scientists will join forces in a greatly expanded effort to determine the nature and function of TAF in order to modify its action.

Monsanto's capabilities for synthesizing and concentrating chemical compounds are expected to be important contributions to the Vallee-Folkman research.

Herbert A. Shaw, a spokesman for the medical school, said that Harvard has never entered into such a relationship before. If it succeeds, it may provide a solution to the recent drastic cutbacks in support from traditional resources.

### Rural Service Required

Medical Tribune World Service

CARACAS—All Venezuelan medical school graduates will be required to spend one year working in small rural towns before being permitted to practice in the cities, under measures now being drafted by the Government.

**"It should be emphasized...that most patients tolerate guanethidine with minimal side effects, when dosage adjustment is carefully managed."**

\*Frela ED, The Modern Management of Hypertension, US Government Printing Office, 1973, pp 13-14.

**when hypertension threatens to outrun control.**

"It should be emphasized...that most patients tolerate guanethidine with minimal side effects, when dosage adjustment is carefully managed."

Often, some of the side effects associated with such drugs as the guanethidine blockers can be avoided by substituting a little Ismelin in the treatment of moderate hypertension.

Because guanethidine is perhaps the most effective antihypertensive agent ever available, Ismelin usually brings blood pressure down to stay. And Ismelin produces no parasympatholytic effects. Further, when used with thiazides, the required addition may be low.

Of course, whenever Ismelin is added to other antihypertensives, initial doses should be small, and increased gradually by small increments.

ments. Once blood pressure control is achieved, all drug dosages should be reduced to lowest effective level, often minimizing side effects.

Patients should be warned about the potential hazards of orthostatic hypotension, and cautioned to avoid sudden or prolonged standing or exercise.

A little extra patient cooperation may be required.

But may well be worth it—for the extra protection Ismelin offers against the dangers of uncontrolled hypertension.

### References

1. Frela ED, The Modern Management of Hypertension, US Government Printing Office, 1973, pp 13-14.  
2. World J Hypertension, 11, 100-101, 1971.  
3. J Am Med Assoc, Philadelphia, PA, September 10, 1972, p 2000.  
4. J Am Med Assoc, Philadelphia, PA, September 10, 1972, p 2000.  
5. J Am Med Assoc, Philadelphia, PA, September 10, 1972, p 2000.

### Ismelin® sulfate

(guanethidine sulfate)

**INDICATIONS:** Moderate and severe hypertension either alone or as an adjunct. **CONTRAINDICATIONS:** Known or suspected pheochromocytoma; hypersensitivity to guanethidine; heart failure due to hypertension; initiation of therapy.

Patients taking Ismelin are a potent drug and can experience side effects. Patients should be warned of the possibility of orthostatic hypotension and advised to avoid sudden or prolonged standing or exercise.

Ismelin should be used with extreme caution in patients with a history of bronchial asthma, since their condition may be aggravated.

**Warnings:** Patients should be warned of the potential hazard of orthostatic hypotension, which can occur frequently and Ismelin should be used in patients only when the risk of hypotension is outweighed by the benefits. Ismelin should be used with extreme caution in patients with a history of bronchial asthma, since their condition may be aggravated.

add a little **Ismelin® sulfate** (guanethidine sulfate)

...because the good is 1/1090

Concurrent use with rauwolfia derivatives may cause excessive postural hypotension, bradycardia, and mental depression.

If possible, withdraw therapy 2 weeks prior to surgery to reduce the possibility of vascular collapse and cardiac arrest during anesthesia. If emergency surgery is indicated, administer Ismelin and analeptic agents cautiously in reduced dosage and have oxygen, atropine, vasopressors, and IV solutions ready for immediate use to treat vascular collapse. Vasopressors should be used with extreme caution in patients on Ismelin because of the possibility of synergistic response and the greater propensity for cardiac arrhythmias.

Dosage requirements may be reduced in the presence of fever, exercise, or other conditions when treating patients with a history of bronchial asthma, since their condition may be aggravated.

**Precautions:** The safety of Ismelin for use in pregnancy has not been established. Therefore, this drug should be used in pregnant patients only when the benefits of treatment clearly outweigh the risks to the fetus.

**Precautions:** Ismelin should be used with extreme caution in patients with a history of bronchial asthma, since their condition may be aggravated.

**Warnings:** Patients should be warned of the potential hazard of orthostatic hypotension, which can occur frequently and Ismelin should be used in patients only when the risk of hypotension is outweighed by the benefits. Ismelin should be used with extreme caution in patients with a history of bronchial asthma, since their condition may be aggravated.

clancy or recent myocardial infarction, cerebral vascular disease, angina pectoris, heart failure, renal impairment, peripheral vascular disease, and aortic aneurysm.

Do not give Ismelin to patients who have severe cardiac failure or who are receiving digitalis therapy. Ismelin may be given to patients with a history of atherosclerosis, but both digitalis and Ismelin should be given cautiously.

Papillary ulcer or other chronic disorders may be aggravated by a relative increase in parasympathetic tone.

Anorectic-amphetamine compounds, amphetamine, epinephrine, naphthylphenol, tricyclic antidepressants (e.g., amitriptyline, imipramine, desipramine), and other sympathomimetic agents may potentiate the effects of Ismelin.

Ismelin should be used with extreme caution in patients with a history of bronchial asthma, since their condition may be aggravated.

**Warnings:** Patients should be warned of the potential hazard of orthostatic hypotension, which can occur frequently and Ismelin should be used in patients only when the risk of hypotension is outweighed by the benefits. Ismelin should be used with extreme caution in patients with a history of bronchial asthma, since their condition may be aggravated.

ing of vision, parotid tenderness, myalgia, muscle tremor, mental depression, orthostatic hypotension, chest constriction, nasal congestion, headache, dizziness, and weakness. Ismelin should be used with extreme caution in patients with a history of atherosclerosis, but both digitalis and Ismelin should be given cautiously.

**Precautions:** Ismelin should be used with extreme caution in patients with a history of bronchial asthma, since their condition may be aggravated.

**Warnings:** Patients should be warned of the potential hazard of orthostatic hypotension, which can occur frequently and Ismelin should be used in patients only when the risk of hypotension is outweighed by the benefits. Ismelin should be used with extreme caution in patients with a history of bronchial asthma, since their condition may be aggravated.

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### Tribune Economic Analysis



**Stocks Running Collision Course With Bond Trend**

The bond market always determines not only the direction of stock market moves but also the timing.

A recent bond report in the *Wall Street Journal* took the form of an interview with the chief credit rater at Standard and Poor's. It quoted him as warning that business generally—and top-rated ones in particular—are underfinanced. It cites him as predicting a still more desperately underfinanced condition for the U.S. Government; he guesstimated that it needs to raise at least \$90 billion this year in the public market.

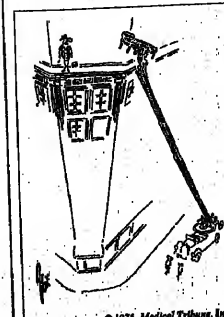
"That will leave precious little for everybody else," the *Wall Street Journal* quotes the Standard and Poor's rater as saying. There's no way the Federal Government can play the heavy as the big pig at the credit trough and still leave enough for the smaller credit users who are its partners in tax collections.

### On Borrowed Time

But the buildup in new demand for bond money and the run-up stock prices are on a collision course. The run-up in stock prices may reverse itself. The buildup in the demand for new bond money is not about to. The trustworthiness for a run-up in stock prices is when no one wants to raise new money. When everyone who can get it needs it, like now, stock prices become suspect. They never run uphill against bond yields for very long.

The stock market is living on borrowed time that is running out in the face of a bond market being broken by Treasury borrowings.

The runway in Government borrowings, plus the underfinanced conditions of the best corporations, guarantees that bond yields will remain at 9 per cent or go still higher. The reversal in stock prices may prove more serious than a mere correction.



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C I B A

## Group B Strep Infections 'a Major Threat' to Newborn

Medical Tribune Report

NEW YORK—Group B hemolytic streptococcal infections have become a major threat to newborn infants throughout the U.S., Dr. Marita D. Yow, Professor of Pediatrics, Baylor College of Medicine, told a National Foundation symposium on fetal and neonatal infections here.

The infantile diseases caused by Group B streptococci, "relatively insignificant" ten years ago, have not replaced in the nursery, Dr. Yow said, but have been added on. For example, the incidence of bacterial meningitis in the newborn at five hospitals in Houston, Texas, which "parallels experience in other cities," has virtually doubled during the last five years, while incidence of infections from other groups of streptococci has not appreciably diminished.

### Broad Spectrum of Illness

The spectrum of illnesses caused by Group B streptococci, she said, ranges from asymptomatic colonization to serious and fatal disease, and includes septicemia, meningitis, arthritis, pneumonia, empyema, osteomyelitis, ethmoiditis, cellulitis and conjunctivitis.

When onset occurs during the first week of life, there is a high mortality rate (60-75 per cent), severe multi-system involvement, and the etiologic agent may be any of five serotypes of streptococci; when onset is after the first week mortality is lower (14-18 per cent), infection is due almost exclusively to type III organisms, and the affected site is mainly the meninges.

According to Dr. Yow, the mode of transmission of infection in the "early onset syndrome" is directly from the mother to the infant; this has been determined by the "complete concordance between the strain of organism harbored in the mother's vagina and the organism her infant was colonized by." The acquisition of infection in "late onset disease" is less clear, but there are suggestive signs that the nursery environment itself is an important source of colonization. A Houston study last year found that the rate of infant colonization by Group B streptococci from just after birth to time of discharge from hospital rose from 22 to 65 per cent.

### Discrepancy With Attack Rate

The same study noted a marked discrepancy between the high infant colonization rate (65 per cent) and the disease attack rate in the infants which was only three per thousand live births (.3 per cent). Dr. Yow stated that there was little known as yet concerning the immune mechanisms that might account for this, but it is recognized that low birth weight and prolonged rupture of maternal membranes do predispose to invasion in "early onset" disease.

Maternal infection with group B streptococci is generally inapparent or expressed as bacteremia or amnionitis with low grade perinatal fever. Bacteriologic isolation and diagnosis are accomplished by growing pure colonies of the infecting organism, extracting the group carbohydrates, and demonstrat-

ing a serological reaction between the extracted antigen and specific grouping antiserum.

### Alternative Method Suggested

Since this procedure may be impractical in the ordinary clinical laboratory, Dr. Yow suggested an alternative method of establishing streptococcal grouping using a battery of five tests: determination of hemolytic activity, bacitracin susceptibility, hydrolysis of sodium hippurate, hydrolysis of esculin in presence of 40 per cent bile, and tolerance to 6.5 per cent NaCl broth.

Where serotyping is required, it can be requested from the Center for Disease Control, where a rapid fluorescent antibody technique for identifying

group B streptococci has also recently been developed.

Whatever strain of B-streptococcus is discovered as the etiologic agent, immediate and vigorous treatment with penicillin is "essential because of the serious and fulminant nature of these illnesses, both in the early- or late-onset syndromes," Dr. Yow said. Penicillin administered intravenously over a period of ten days will eradicate most of the organisms from the blood, spinal fluid, and other foci, she said, although tissue damage may be irreparable and the throat and rectum may continue to harbor the organism.

Besides "vigilant cleanliness and scrupulous hand-washing on the part of nursery personnel, there were no

prophylactic or preventive measures against infant B-streptococcal disease that Dr. Yow could recommend at present.

Routine treatment of vaginally colonized pregnant females with penicillin could not be justified, in view of the widespread prevalence of colonization and antibiotic side-effects, she said. "You would have to treat 500 adults per 1,000 live births for a disease whose attack rate is no more than three in a thousand," Dr. Yow pointed out "and even then, we know that late-onset disease can be acquired neonatally."

Instead she called for more investigation into the factors that influence the ecology of the maternal vagina, changes in herd immunity, virulence as related to serotype, and the natural history of the carrier state.

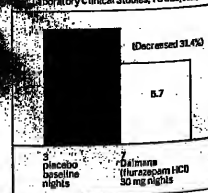
B.O.

## Would sleep with fewer nighttime awakenings benefit your patients with insomnia?

Highly predictable results for your patients with trouble staying asleep...

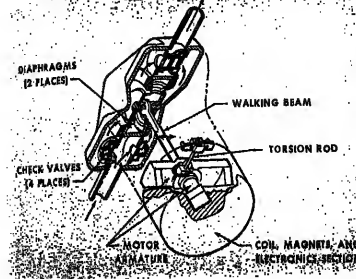
...can be obtained with Dalmane (flurazepam HCl). As shown below, Dalmane significantly reduces nighttime awakenings.<sup>1,4</sup>

Average Number of Nighttime Awakenings<sup>1,4</sup> in Geographically Separated Sleep Research Laboratory Clinical Studies, 16 Subjects



Wednesday, April 23, 1975

## NASA Pump Adaptable to Heart-Lung Systems Disrupts Fewer Red Blood Cells



In the Apollo pump two Dacron diaphragms, coated with butyl rubber, are attached at the end of an oscillating beam mounted on a torsion bar. Each diaphragm covers a chamber equipped with inlet and outlet check valves. When one diaphragm is pressurized, its chamber, thereby opening its outlet valve, the other diaphragm is providing suction to the alternate chamber opening its inlet valve. When the oscillating beam moves in the opposite direction, each chamber reverses its function.



And for those with trouble falling asleep or sleeping long enough...

...Dalmane (flurazepam HCl) also delivers excellent results. Clinically proven in sleep research laboratory studies: on average, sleep within 17 minutes that lasts 7 to 8 hours.<sup>2</sup>

Dalmane (flurazepam HCl) is relatively safe, seldom causes morning "hang-over" and is well tolerated. The usual adult dose is 30 mg a.s., but with elderly and debilitated patients, limit the initial dose to 15 mg to preclude oversedation, dizziness or ataxia. Evaluation of possible risks is advised before prescribing.

### REFERENCES:

1. Karesen I, Williams RL, Smith JR: The sleep laboratory in the investigation of sleep and sleep disturbances. Scientific exhibit at the 124th annual meeting of the American Psychiatric Association, Washington DC, May 3-7, 1971.
2. Pratt JD Jr: A system for automatically analyzing sleep. Scientific exhibit at the 24th Annual Clinical Convention of the American Medical Association, Boston, Nov 29-Dec 2, 1970, and at the 42nd annual scientific meeting of the Aerospace Medical Association, Houston, Apr 26-29, 1971.
3. Vogel GW: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ.
4. Demant WC: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ.

Before prescribing Dalmane (flurazepam HCl), please consult complete product information, a summary of which follows: Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended. Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage. Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypotensive or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function. Adverse Reactions: Dizziness, drowsiness, light-headedness, staggering, ataxia and falling have occurred, particularly in elderly

or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, irritability, apprehension, irritability, weakness, palpitations, chest pain, body and joint pains and GU complaints. There have also been rare occurrences of sweating, flushing, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, incoherence, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, e.g., excitement, stimulation and hyperactivity, have also been reported in rare instances. Dosage: Individualize for maximum beneficial effect. Adults: 30 mg usual dosage. 15 mg may suffice in some patients. Elderly or debilitated patients: 15 mg initially until response is determined. Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

Depend on highly predictable results with **Dalmane** (flurazepam HCl) specifically indicated for insomnia

Objectively proved in the sleep research laboratory:  
 • sleep with fewer nighttime awakenings  
 • sleep within 17 minutes, on average  
 • sleep for 7 to 8 hours, on average, with a single a.s. dose.



ROCHE LABORATORIES  
 Division of Hoffmann-La Roche Inc.  
 Nutley, New Jersey 07110

BOSTON—A pump originally designed to circulate fluids in astronauts' space suits is being tested for use in extra-corporeal heart-lung systems and "could conceivably" make it possible for the heart to be bypassed for an indefinite number of days or weeks, a team of scientists reported at a meeting of the Association for the Advancement of Medical Instrumentation.

The Apollo double diaphragm pump (ADDP), which is also being investigated for adoption in implantable artificial heart-lung systems, is significantly less destructive to red blood cells than any existing pump now used in heart-lung machines, the team reported. These findings were based on

Continued on page 23

## Doctors Are Alerted To Tick Typhus Rise

Medical Tribune Report

NEW ORLEANS—With the approach of the late spring and summer outdoor season, physicians should suspect tick typhus, or Rocky Mountain spotted fever, when confronted with an acute febrile exanthematous illness—especially in a woman or child, the Pediatric Pathology Club was told here.

An unprecedented 774 cases of the disease were reported last year by the Public Health Service, 416 of them in the South Atlantic states where tick typhus is endemic, according to Dr. Hal K. Hawkins of Duke University School of Medicine. In 1973 the national total was 638 cases, the previous record.

Dr. Hawkins, a pathologist, warned that the typhus may be mistaken for measles and meningococcemia.

He reported to the Club on experience with 120 children who were treated at Duke over the last 30 years. All had the clinical hallmarks: fever, rash, and a history of tick bite. Hyponatremia was present in 43 of 49 children tested, reflecting the increased vascular permeability characteristics of the disease. Thrombocytopenia was present in 25 of 33 patients in whom quantitative platelet counts were made. Findings at autopsy reflected generalized vasculitis.

Dr. W. D. Bradford is in charge of the Duke study. Dr. C. R. Abramo-sky and Dr. Hawkins are his associates.

## MBD Case History #1

# 1971...a difficult child, a distraught mother

## Medical diagnosis: MBD.



Robert Boynton,\* second of five children, born October 7, 1963. Normal pregnancy and delivery.<sup>1</sup>

From the age of 3, Robert's mother found him "hard to handle," "wilder" than his brothers and sisters.<sup>1</sup>

At age 6, after an "extremely difficult" experience in kindergarten, Robert was referred to a pediatric neurologist. The examination and later psychological testing revealed a host of the neurologic "soft signs," plus an abnormal EEG.<sup>1</sup>

The diagnosis: average intelligence, but multiple signs of an underlying organic dysfunction.<sup>1</sup>

At age 7, Robert was placed in a special first-grade class called an "extended readiness program."<sup>2</sup>

Later that year, her child's continued problems at school and at home made Robert's mother "increasingly desperate" for help.

## An MBD child on the road to maturity

### Ritalin® hydrochloride C (methylphenidate hydrochloride)

**INDICATIONS**  
Minimal Brain Dysfunction in Children—as adjunctive therapy to other remedial measures (psychological, educational, social).  
**See also Diagnostic Considerations.**  
Specific etiology of Minimal Brain Dysfunction (MBD) is unknown, and there is no single diagnostic test. Adequate diagnosis requires the use not only of medical, but of special psychological, educational, and social resources.  
Characteristics commonly reported include: chronic history of short attention span; distractibility; emotional lability; impulsivity and moderately to severely hyperactivity; minor neurological signs and symptoms. EEG Learning may or may not be impaired. The diagnosis of MBD must be based upon a complete history and evaluation of the child and not solely on the presence of one or more of these characteristics. Drug treatment is not indicated for all children.

with MBD. Stimulants are not intended for use in the child who exhibits symptoms secondary to environmental factors and/or primary psychologic disorders, including psychosis. Appropriate educational placement is essential and psycho-social intervention is generally necessary. When remedial measures alone are insufficient, the decision to prescribe stimulant medication will depend upon the physician's assessment of the chronicity and severity of the child's symptoms.

**CONTRAINDICATIONS**  
Marked anxiety, tension, and agitation, since Ritalin may exacerbate these symptoms. Also contraindicated in patients known to be hypersensitive to the drug and in patients with glaucoma.

### WARNINGS

Ritalin should not be used in children under six years of age, since safety and efficacy in this age group have not been established.  
Safe use of Ritalin in children with minimal brain dysfunction are not yet available. Although apparent growth has not been established, weight gain and/or height has been reported with long-term use of Ritalin in children. Therefore, children receiving long-term therapy should be carefully monitored.

Ritalin should not be used for severe depression of either endocrine or autonomic origin or for the prevention of normal lactation states.

Patients may lower the convulsive threshold in patients with or without prior seizures with or without prior EEG abnormalities, even in the absence of seizures. Safe concomitant use of Ritalin and anticonvulsants has not been established.

If seizures occur, Ritalin should be discontinued. Ritalin should be discontinued if seizures occur.

Use cautiously in patients with hypertension. Blood pressure should be monitored at intervals.

at intervals in all patients taking Ritalin, especially those with hypertension.  
**Drug Interactions**  
Ritalin may decrease the hypotensive effect of guanethidine. Use cautiously with pressor agents and MAO inhibitors. Ritalin may inhibit the metabolism of coumarin anticoagulants, antiarrhythmics, anticholinergics, and tricyclic antidepressants, and may potentiate the effects of these drugs. Therefore, when these drugs are used concurrently with Ritalin, dosage adjustments of these drugs may be required when given concurrently with Ritalin.  
**Use in Pregnancy**  
Adequate animal reproduction studies to establish safe use of Ritalin during pregnancy have not been conducted. Therefore, Ritalin should not be used in pregnant women unless the potential benefits outweigh the possible risks.

# 1974...a regular fourth-grader, accepted at home

In the opinion of the physician, methylphenidate (Ritalin) was called for to help the child over the obstacles of hyperactivity. So he initiated a trial of the drug, which was then implemented on school days only.<sup>1</sup>

The improvement in classroom performance and behavior was "prompt and dramatic." Robert's teacher could "scarcely believe" that he was the same child.<sup>1</sup>

For the past 4 years (as of April 1974), Robert has been maintained on 15 mg methylphenidate daily during school periods. During the summer he attends day camp and is not on medication. He is in a regular fourth-grade class, and behavioral problems at home have lessened. Robert's parents now find it much easier to accept their son.<sup>1</sup>

**\*Note:** In this presentation, clinical material has been used factually with the permission of the physician. However, identities have been concealed and names changed.

**How other children with MBD can benefit from methylphenidate therapy**

Of course, medication is not indicated for all MBD children; nor will all such children respond to drug therapy.

However, when pharmacotherapy is clearly indicated, the use of a widely successful drug such as Ritalin (methylphenidate) may prove to be a significant element in many complete remedial programs.

Over a decade of controlled studies has underlined the beneficial effects of Ritalin in producing improved behavior ratings,<sup>2,3</sup> better motor coordination,<sup>2,4</sup> and cognition and learning.<sup>2,4</sup> Indeed, it is currently the drug of choice in many MBD situations.<sup>5</sup>

And side effects with Ritalin have occurred less frequently than with other stimulant drugs.<sup>6,7</sup> Dosage should be periodically interrupted in the presence of improved motor coordination and behavior. These interruptions often reveal that the child's behavior shows some "stabilization" even without chemotherapy, permitting a reduction in dosage and gradual elimination of drug therapy.

Of course, Ritalin is not indicated for childhood personality and behavioral disorders not associated with medical diagnosis of MBD.



# Ritalin® (methylphenidate)

## can help when medication is indicated

**Drug Dependence**  
Ritalin should be given cautiously to emotionally unstable patients, such as those with a history of drug dependence or alcoholism. Because such patients may increase dosage on their own initiative, periodic physical exams can be used to detect tolerance and psychic dependence with Ritalin. Ritalin should not be used in patients with a history of drug dependence or alcoholism. Ritalin should not be used in patients with a history of drug dependence or alcoholism.

**ADVERSE REACTIONS**  
Nervousness and insomnia are the most common adverse reactions but are usually controlled by reducing dosage and omitting the drug in the evening. Other reactions include: anorexia, weight loss, dry mouth, urinary hesitancy, constipation, dermatitis, arthralgia, myalgia, headache, dizziness, blurred vision, tachycardia, palpitations, blood pressure changes, both up and down, orthostatic hypotension, cardiac arrhythmias, epistaxis, and weight loss during prolonged therapy. Toxic psychosis has been reported. Although a definite causal relationship has not been established, the following have been reported in patients taking the drug: irritability and/or anorexia; a new instance of acute hair loss; in children, loss of appetite, abdominal pain, weight loss during prolonged therapy, irritability, and tachycardia. In some cases, these reactions have been reported in patients taking the drug.

**DOSEAGE AND ADMINISTRATION**  
Children with Minimal Brain Dysfunction (6 years and over):  
Start with small doses (eg, 5 mg before breakfast and lunch) with gradual increments of 5 to 10 mg weekly. Do not exceed 60 mg in 24 hours. If improvement is not observed after a one-month period, the drug should be discontinued. If adverse effects occur, reduce dosage, or if necessary, discontinue the drug.  
Ritalin should be periodically discontinued to assess the child's condition. Improvement may be maintained when the drug is discontinued. Drug treatment should not be discontinued after a prolonged period of therapy.

**HOW SUPPLIED**  
Ritalin (methylphenidate hydrochloride) tablets, 5 mg (pink, scored) bottles of 100, 500, 1000, and 2000.  
Ritalin (methylphenidate hydrochloride) capsules, 10 mg (pink, scored) bottles of 100, 500, 1000, and 2000.  
Ritalin (methylphenidate hydrochloride) syrup, 10 mg (pink, scored) bottles of 100, 500, 1000, and 2000.  
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